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INTRODUCTION TO HUMAN PARASITOLOGY

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INTRODUCTION TO HUMAN PARASITOLOGY

BY

ASA C. CHANDLER, M.S., Ph.D.
Professor of Biology, Rice Institute, Houston, Texas. Formerly Officer-in-charge, Hookworm Research Laboratory, School of Tropical Medicine and Hygiene, Calcutta, India.

FOURTH EDITION

REWRITTEN AND ENLARGED, SUPERSEDING
ANIMAL PARASITES AND HUMAN DISEASES

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To
MY MOTHER
WHOSE SELF-DENYING LOVE AND UNFAILING
DEVOTION MADE MY SCIENTIFIC
EDUCATION POSSIBLE

PREFACE

Twelve years ago the writer prepared a book on " Animal Parasites and Human Disease " which was designed to set forth the important facts of human parasitology in a form which was sufficiently non-technical, and sufficiently readable, so that it would be both useful and stimulating to a wide range of readers who, for one reason or another, might be interested in the subjects dealt with by the book. Among those who were considered as possible readers were public health and immigration service officers, physicians whose interest extended beyond the comparatively narrow limits of a local practice, teachers of hygiene, of domestic science, or of other subjects in which a knowledge of parasitology might have a bearing, college and high school students who wanted an introductory knowledge of the subject, and also travelers and other non-professionals who were interested in the progress of a rapidly developing branch of science that has an important bearing on human welfare, but that was nowhere so presented as to be intelligible to a lay reader.

It was felt by the writer that there was a tendency for scientists to blaze trails into unknown territory at so rapid a rate that the general public was being left too far behind, with the result that it was becoming more and more difficult for any but specialists to understand the importance or significance of new discoveries, or to make efficient use of older ones. Not only does this in many instances lessen the utilitarian value of discoveries which, if generally understood and made use of, would contribute to the welfare of mankind, but it also makes the further progress of the scientist steadily more difficult. With rare exceptions scientific work finds fewer obstacles when it has an approving public sentiment behind it. Such a sentiment can scarcely be expected if results already achieved are not capitalized and an intelligent understanding of results hoped for is not fostered. Popular ignorance of many important facts of parasitology and preventive medicine, even facts which have been common bases of operation for scientists for many years, is deplorable. To a large extent the scientists themselves are responsible for this condition, for in their enthusiasm for further discoveries they have neglected to make it possible for the human race in general to reap the benefits of their earlier ones to the largest extent possible. It was with these thoughts in mind that " Animal Parasites and Human Disease " was written as a popular treatise on a little-

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understood subject, for the benefit of the general public as well as the student. The intervening years have shown that an attempt to educate the public directly in this field of scientific endeavor was premature. The book was not extensively bought or read by the general public, but it *was* widely adopted as a textbook for introductory courses in parasitology, both in academic and medical schools, and has gone through three editions. Inasmuch as improvement for this purpose could be attained by giving up what now appears to have been a futile attempt to make it serve an even wider purpose, the book has been entirely rewritten and rearranged from this point of view, and is now being offered, as a textbook, under its new name, "Introduction to Human Parasitology."

The writer's faith in the value of popular education in the subject has not faltered, but his idea of the method by which this result can be obtained has changed. It is felt that, instead of presenting the subject directly for the general public, more good can be accomplished by presenting it indirectly, through college and university students. The information contained is detailed enough to serve as an introductory text for students who are going into medical or public health work. On the other hand it has been the writer's endeavor to present the information in such a way as to interest other students, who may elect the subject as a cultural course, to widen their range of knowledge and interests, just as it can be widened by a study of history, literature, sociology or other " cultural " subjects. Many academic students become teachers. For these a knowledge of parasitology will inevitably prove valuable, not only as a source of instructive material on which to draw in teaching biological and hygienic courses, but also for practical purposes in connection with local problems in sanitation and hygiene, with which the teacher always comes in contact. It is the writer's opinion that a course involving the essential facts of parasitology and bacteriology should be offered for academic students as an elective course in every first-class college and university, for these subjects have more bearing on everyday life, and more practical and useful interest for the average citizen, than have many of the advanced biological courses now available.

In a broad sense, parasitology includes a study of parasites of both animal and vegetable nature, but in common practice it is restricted to a study of animal parasites only, the vegetable ones being considered under the head of bacteriology, as a sister subject. It is in the restricted sense that the word is here used. The exact limits of parasitology, in its restricted sense, are difficult to determine, for on two of its borders it merges with other domains. On one side it merges with its sister subject, bacteriology, and there are groups of organisms which might be, and in fact are, considered in either field or in both. Such, for instance, are the spirochætes and rickettsiæ. Although there is no sound reason for considering these as animals rather than bacteria, the methods of working with them, and the way in which they behave with reference to their hosts, do to some extent ally them with the protozoa, and in most bacteriology texts they are shamefully neglected. For these reasons, rather than from any conviction of their animal nature, it has seemed desirable to include them in this book. On the opposite border, animal parasitology merges with medical entomology. There is no definite boundary line between insects which are strictly parasites, such as lice and fleas, and insects such as mosquitoes and tabanids, which are not parasitic in habitat but are parasitic in their food habits. In this book there have been included not only those insects which habitually live on or in the body in some stage of their development, but also those which habitually suck blood; particular emphasis is laid on those forms which serve as common vectors for disease germs. Non-blood-sucking insects which are not parasites even in the broadest sense, such as house flies and roaches, even though they come into prominence in medical entomology as mechanical conveyors of disease germs, are not included, and this is also true of merely poisonous insects, which are in no sense parasites.

The book has been divided into three main sections, dealing respectively with protozoa, helminths and arthropods. Within these sections the chapters have been arranged, in the main, in a systematic manner from the standpoint of classification, but it has not been deemed advisable to follow this out in all cases. For example, it seemed to the writer preferable to group together the intestinal flagellates and ciliates in one chapter, to deal with the various flukes according to their habitat in the body rather than their zoölogical affinities, etc.

No attempt has been made to give complete descriptions of all the parasites dealt with, though in those cases where it is particularly important to avoid confusion between two important species, *e.g.*, between *Endamœba histolytica* and *E. coli*, between *Tænia solium* and *T. saginata*, and between *Xenopsylla cheopis* and *X. astia*, sufficiently detailed descriptions or figures have been given to make a correct identification possible. The classification has not been emphasized, and only a sufficient outline has been given in the different groups to give an adequate comprehensive view, and to give a correct idea of the general relationships of the organisms dealt with. Discussions of correct scientific names and synonymy have been omitted because in the writer's opinion they have no place in an introductory text. An effort has been made to use scientific names which are most generally accepted as correct, except that in cases of disagreement between American and European usage the American name has been used. In cases where some name or names other than the one now accepted as correct under the rules of zoölogical nomenclature have long been in common use, these names are given in parentheses.

Throughout the book special emphasis has been laid on the biological aspects of the subject. Considerable space is devoted to life cycles, epidemiological factors, inter-relations of parasite and host, and underlying principles of treatment and prevention, rather than on such phases as classification, nomenclature, morphology, etc., which occupy most of the space in some textbooks of parasitology. The book is an introductory one, and as such endeavors to give a knowledge of fundamental facts and principles rather than merely a compilation of selected important details. Some of the teachers who have used the forerunner of this book suggested that the sections on treatment might be left out entirely. So far as specific and detailed directions for treatment are concerned, this has been done; it is, however, properly within the scope of an introductory book on parasitology to discuss the general *principles* of treatment, such as the specific reaction between certain parasites and certain drugs, the manner in which drugs reach the parasites, the mechanism by which the effect is brought about, and factors which contribute to success or failure. These are true biological aspects of the subject.

Parasitology has grown so rapidly in recent years, and covers such a wide field, that it is difficult to go very far into the subject within the limits of one book. Nevertheless it is the writer's belief that a comprehensive integrated account of the entire field is much the most desirable method of approaching the subject at the start. Protozoölogy, helminthology and medical entomology have many inter-relations, and no one of them can be satisfactorily pursued very far without some knowledge of the others. But for more advanced work a comprehensive text is too cumbersome; the subject naturally splits into its three component parts. There are excellent up-to-date textbooks available in protozoölogy and helminthology, though there is no entirely satisfactory modern book in medical entomology. For the parasitologist who wishes to continue in the protozoölogical field, Wenyon's "Protozoölogy" (2 volumes) or Knowles' shorter "Introduction to Medical Protozoölogy" can be especially recommended; and for the helminthologist, Faust's "Human Helminthology." These books are up-to-date and thorough, and contain excellent bibliographies from which the student can get a clue to the literature on any subject falling in these fields. It was originally intended to add a bibliography to the present text, but since the bibliography is needed only for students who intend to follow the subject further, and since the books mentioned are essential as references for such students, it seemed useless to repeat, or select from, the bibliographies contained in these more advanced books. Frequent reference to names of investigators and dates have, however, been made in the text, the purpose being mainly to familiarize the student with the names of a few of the leading men who have made important contributions to the subject under discussion, and to give him an historical background. At the end of the book is a list of " Sources of Information " containing a list of the leading journals in which important articles on parasitology frequently appear, and a list of books which cover all or a portion of the field of parasitology in a comprehensive manner. Most of these books contain bibliographies, and most of the references cited in these bibliographies will be found in the journals listed.

If it is desired to keep in touch with important new discoveries in parasitology, which are constantly being made, and some of which will undoubtedly have appeared even before this book can make its first appearance, reference to current numbers of such of these journals as are available will be of great help. Particular attention is called to three of these publications — the *Tropical Diseases Bulletin,* which reviews practically all current work in the field of human parasitology, especially protozoölogy and helminthology; the *Review of Applied Entomology, Series B,* which contains abstracts of all important work on medical and veterinary entomology; and the *Journal of the American Medical Association*," which gives references to all articles in the leading medical journals of all countries, and reviews many of them. Any of the reprints or pamphlets received by the Bureau of Hygiene and Tropical Diseases, which publishes the *Tropical Diseases Bulletin,* will be sent on loan to any part of the world when directly applied for, and the American Medical Association will likewise loan any of the periodicals in its library to any member of the Association. The three periodicals mentioned, on account of their scope and thoroughness, are of inestimable value to any one who attempts to keep pace with the progress of parasitology.

The writer takes pleasure in acknowledging the great assistance which he has obtained from these journals in the preparation of this book, which in fact could not possibly have been done without them. There are, however, few if any of the journals or books listed under " Sources of Information " which have not been drawn upon either for information or illustrations, or both. All of them, collectively, have made this book possible, and to them, and to the workers who contribute to them, are due, therefore, not only the thanks of the writer, but also the thanks of everyone who may profit in any way by the present volume.

The forerunner of the present book, " Animal Parasites and Human

Disease," was very kindly read by three eminent authorities, who freely gave the benefit of helpful suggestions and criticisms, namely Professor Gary N. Calkins, Professor of Protozoölogy at Columbia University, the late Dr. B. H. Ransom, of the Zoölogical Division of the U. S. Bureau of Animal Industry, and Dr. L. O. Howard, Chief of the U. S. Bureau of Entomology, since retired. These men helped materially to round off the rough corners, and fill in the chinks, of the sections on protozoa, " worms " and arthropods, respectively. The benefits of their assistance have been carried on into the present book. The writer also expresses his appreciation for suggestions made by Dr. M. A. Stewart, of the Rice Institute, in connection with the section on arthropods. Hearty thanks are also due my wife, Ina Sands Chandler, for valuable help in the editorial part of the work.

ASA C. CHANDLER.

HOUSTON, TEXAS,
September, 1929.

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INTRODUCTION TO HUMAN PARASITOLOGY

CHAPTER I

INTRODUCTION

One of the most appalling realizations with which every student of nature is brought face to face is the universal and unceasing struggle for existence which goes on during the life of every living organism, from the time of its conception until death. We like to think of nature's beauties; to admire her outward appearance of peacefulness; to set her up as an example for human emulation. Yet under her seeming calm there is going on everywhere — in every pool, in every meadow, in every forest — murder, pillage, starvation and suffering.

Man often considers himself exempt from this interminable struggle for existence. His superior intelligence has given him an insuperable advantage over the wild beasts which might otherwise prey upon him; his inventive genius defies the attacks of climate and the elements; his altruism, which is perhaps his greatest attribute, protects, to a great extent, the weak and poorly endowed individuals from the quick elimination which is the inevitable lot of the unfit in every other species of animal on the earth. Exempt as we are, to a certain extent, from these phases of the struggle for existence, we have not yet freed ourselves from two other phases of it, namely competition among ourselves, resulting in war, and our fight with parasites, resulting in disease. Since the last great conflagration of war has burned itself out and its ashes, the flesh and bones of its countless victims, have disintegrated and disappeared from view, our statesmen have been devoting themselves as never before to an effort to prevent it from recurring again — with what success only the future can tell. Meanwhile our scientists have been devoting themselves to freeing us from the helpless bondage in which we were once held by the organisms of disease, and the outlook here is definitely brighter. One by one the diseases which formerly held the world in terror, or made parts of it practically uninhabitable, are falling before the onslaught of modern science and research. With few exceptions, so far as man is concerned, the enemy has been discovered, his resources and limitations are known, and his tactics understood. Smallpox, before the days of vaccination, missed scarcely five people in a hundred, and a fourth of those attacked died; today smallpox is almost gone from civilized countries. Plague, before its manner of dispersal was known, once spread over Europe in a devastating epidemic which killed one-fourth of its population — some 25,000,000 people; today when the disease does sneak into a new territory in a civilized country, as it has done in recent years in California and our Gulf coast, its victims are numbered in dozens. Yellow fever, before the rôle of mosquitoes was known, periodically terrorized nearly every sea coast city in America; today yellow fever is all but gone from the entire Western Hemisphere. In the last century malaria and yellow fever made Panama a pest hole which came to be known as the "white man's graveyard," and caused the French attempt to build a canal to end in dismal failure, with horrible loss of life; today the Canal Zone is one of the healthiest places in the world, and the "conquest of the tropics" has been proved both possible and profitable. Similar changes in many other diseases — typhoid, cholera, typhus, wound infections, etc., — could be cited. Some of these diseases are bacterial, and their conquest is due to the brilliant work of our bacteriologists since the time of Pasteur. Others are caused by animal parasites, or are transmitted by parasites or blood-sucking insects; — their downfall is credited to advances in knowledge in animal parasitology and medical entomology; it is with this phase of the question that the present book deals. Many of the parasitic infections are not of such spectacular significance to the human race as some of those mentioned above, but in the aggregate their importance is enormous. No one questions the importance of malaria, trypanosomiasis, kala-azar, amebic dysentery, relapsing fever, hookworm, filariasis, scabies, or of the attacks of disease-transmitting mosquitoes, lice and fleas. But even many of the lesser lights among parasites, of rarer occurrence or of local distribution, are of importance to the human race far out of proportion to popular interest or knowledge of them. In China 10,000,000 people are yearly exposed to infection with *Fasciolopsis buski;* in Egypt the vitality of the entire nation is sapped by schistosomes; in western India one-fourth the population of innumerable villages are incapacitated for a month each year by guinea-worms; in our Northwest rich valleys are uninhabitable because of the prevalence of spotted fever, transmitted by ticks. Yet how many educated people have ever even heard of these infections? The affairs of people in foreign countries is no longer inconsequential to us. The human animal, endowed by nature with a wanderlust and an itchy foot, is today traveling farther, faster and oftener, by fast trains, ocean liners and aeroplanes, than he has ever traveled before. Even in the old days when a trip from continent to continent took weeks or months, the dispersal of parasites was common. The ancient traders of Egypt and Syria, searching the Far East for spices and pearls, brought back with them filariæ; centuries later the Europeans, exploring America for gold, brought back syphilis; negroes, brought from Africa as slaves, very likely introduced yellow fever, hookworm, schistosomes, guinea-worms and filariæ to the Western Hemisphere. Within the memory of the present generation Finns and Scandinavians, coming to Canada to help in lumbering operations, left the broad tapeworm to flourish among the dogs and fish of the Canadian woods, — a constant and perhaps ineradicable menace to all present and future Americans who partake of lake fish. It is worth a passing thought that, after years of absence, rabies was re-introduced into England by a dog brought from France in an aeroplane. Parasitic diseases are no longer looked upon as peculiar to the tropics. France has some of the most highly malarial territory in the world, and the dysentery ameba occurs with discomforting regularity in some 10 per cent of the inhabitants of the United States.

With the progress of civilization, however, many human parasites are gradually falling by the wayside, and many of them are doomed. In part this is the result of conscious effort to eradicate them, but in part it is incidental to sanitary improvements with civilization; sanitation has already eliminated many parasites from the progressive countries of the North Temperate zone, and the tropics are slowly but surely following suit. M. C. Hall says "The welfare of the louse was imperilled when the Saturday night bath supplanted occasional immersion from falling into the water, and the louse was doomed when American plumbing laid the foundation for a daily bath or even a morning and night tub a day. Shaving deprived the human ectoparasite of a protected forested area. *Tænia solium* took the road to extinction when the mythical Chinaman burned down the house, and ate the incinerated pig and pronounced it good, and has had no chance against a meat inspection system which tanks all cases of *Cysticercus cellulosæ*. The substitution of the privy and toilet for the rush-covered floor of the Middle Ages spelled present extinction for human ascarids and hookworms. . . . The city water supply does not serve the parasite as does the pond and stream." Without any special campaigns to eradicate them, cooties and worms have become almost negligible factors in the civilized countries of the North Temperate zone; the cook, the barber, the laundryman and the plumber have made their lives too insecure.

As Hall points out, man is, in this respect, in a far better situation than his domestic animals. The latter soil their table with their feces;

they must eat uncooked food and drink largely from ponds and streams; their hairy bodies provide ideal playgrounds for ectoparasites; and their bathing habits are those of the small boy — compulsory baths only, as a rule. Their domestication and increasing concentration leads to increasing parasitization. Under the law of chance, says Hall, the parasite egg that had to pursue its host to a new bed-ground five miles away was out of luck, whereas when millions of eggs are sowed on limited pastures, the parasites have all the advantage. In the case of human parasites, increased concentration has a directly opposite effect, due to improved water supplies, control of foods, and sanitary sewage disposal.

But let us not think for a moment that the battle is won. Not only are there some diseases which still baffle our attempts to cure them or to control them, or even to understand their nature, but those which we already know how to control are by no means subdued. Plague continues to take a toll of life in India amounting to at least several hundreds of thousands a year; malaria even today destroys directly or indirectly millions of people every year, and more or less completely incapacitates many millions more; syphilis is yet one of the principal causes of insanity, paralysis, still-births and barrenness in the civilized world, and is estimated to exist in 6.7 per cent of the population of the United States, *i.e.*, in about 8,000,000 people; hookworms still infect and render more or less imperfect over half a billion people in the world; — and these are all diseases the causes of which are known, the means of transmission recognized, methods of prevention understood, and the cure of which, with the exception of plague, is entirely possible.

It is evident that the crying need of the present time is not so much additions to our knowledge of the cause, control and prevention of diseases, much as this is to be hoped for, as it is the efficient application of what we already know. Popular ignorance of parasitic diseases, even such common ones as malaria and hookworm, is appalling, even among otherwise educated people. People with erroneous or distorted views publish their ideas and are believed; there are medical men, fewer, fortunately, each year, who fail to keep in touch with the rapid advances made, and practice the medicine of 20 years ago; and there are quacks who, like buzzards, prey on the innate gullibility of the human species, and willfully scatter seeds of misinformation. In addition to this, such is the imperviousness of our kind to new ideas, it takes decades, if not centuries, to modify or correct popular notions. One need only mention the popular disbelief in evolution, the credulity with respect to the origin of “ horse-hair snakes ” from horse hairs in water, and the existence of anti-vaccination societies to denounce vaccination as an impractical and illogical proceeding. Little wonder that popular skepticism still exists with respect to the transmission of malaria by mosquitoes, and that people still fear the miasmas of damp night air.

History. Although some of the larger and more conspicuous parasites could not escape the attention of the ancients, parasitology really began about the middle of the 16th century, when the idea began to sprout that disease was due to organisms living and multiplying in the body. Two centuries later Plenciz, a physician of Vienna, apparently with the tongue of a prophet, expressed the idea that all infectious diseases were caused by living organisms, that there was a special "germ" for each disease, that the incubation period of diseases was due to the time required for the infecting organisms to multiply, and that the organisms might be conveyed through the air as well as by direct or indirect contact. Meanwhile the invention of the microscope by the Dutch lens-grinder, Leeuwenhoek, made possible the actual observation of minute "animalculæ" in rainwater, saliva, feces, etc. In the 18th and 19th centuries there was much dispute as to the origin of germs, but one by one the last straws to which the sinking theory of spontaneous generation was clinging were removed, until finally Pasteur removed the last one in 1860.

Naturally, the first development in parasitology was the discovery and description of the parasites. The first parasitic protozoan to be discovered and recognized as such was the ciliate, *Balantidium coli*, found by Malmsten in 1856. The spirochæte of relapsing fever was discovered by Obermeier in 1873; the dysentery ameba by Lösch in 1875; the malaria parasite by Laveran in 1880; the trypanosome of sleeping sickness by Forde and Dutton in 1901; the parasites of kala-azar by Leishman and Donovan, independently, in 1903; the spirochæte of syphilis by Schaudinn, and of yaws by Castellani, in 1905; the leptospira of infectious jaundice by Inada and Ido in 1915; and the rickettsia of typhus by Rocha-Lima in 1916. Of the commoner worm parasites some, such as certain tapeworms, ascaris, oxyuris and guinea-worms, have been known since ancient times, not so much on account of their size as because of their habit, at times, of making their way out of the body where they could not easily escape observation. Trichuris was discovered by Roederer in Germany in 1760; in 1780 a scientific society was founded in Copenhagen to investigate the nature and habits of hydatid cysts, and two years later Goeze, finding hooks and suckers as in bladder-worms, showed their relation to tapeworms. In 1810 Rudophi divided tapeworms into two classes, one of which included what we now recognize as adult tapeworms, the other cystic forms, which were shown to be immature tapeworms over 40 years later;

the trichina worm, in its larval stage, was discovered by Peacock in 1828; hookworms by Dubini in Italy in 1838; *Fasciolopsis* by Busk in 1843; schistosomes and dwarf tapeworms by Bilharz in Egypt in 1851; filaria (larvæ) by Demarquay in 1863; the Chinese liver fluke by MacConnell in India and McGregor in Mauritius in 1874; the adult filaria by Bancroft in 1876; and *Strongyloides* by Normand in the same year. Most of the arthropod parasites and disease transmitters have, of course, forced their attention on mankind since the dawn of his existence, but careful distinctions between species have been made only within the last century.

Experimental methods in parasitology began in 1850, when Herbst succeeded in transmitting trichina by feeding infected meat to animals. In 1852 Kuchenmeister set a new mile post when he discovered, by feeding bladder-worms of rabbits to dogs, that bladder-worms are developmental stages in the life cycle of tapeworms; two years later he proved that bladder-worms in pigs gave rise to tapeworms in man, as he had suspected on account of the similarity of their heads. In the last half of that same decade Virchow and Leuckart worked out the life cycle of *Trichinella* and Zenker proved its clinical importance. In 1862 Leuckart proved the relationship of hydatid cysts and minute tapeworms in dogs. In the seventies, Lewis, in India, found microfilariæ in the blood, and associated their presence with elephantiasis and other diseases, and Manson, in China, showed that further development of the embryos occurred in *Culex*, but it was not until 1900 that Low showed how the infection took place. The following decade brought a demonstration by Perroncito of the injuriousness of hookworm, and a partial solution of the life cycle of the broad tapeworm by Braun. In 1883 Thomas and Leuckart both worked out the complete life cycle of the liver fluke, *Fasciola hepatica*, though Weinland, nearly ten years before, had found cercariæ in snails which he believed to belong to this species, and the life cycles of other flukes had already been discovered.

The decade from 1890 to 1900 was another outstanding one. In 1893 Smith and Kilbourne proved that Texas fever of cattle was transmitted by ticks. This was the first demonstration of the instrumentality of insects in transmission of protozoan diseases. Two years later Bruce showed that *Trypanosoma brucei* was transmitted by tsetse flies, a discovery which paved the way for proof of the rôle of tsetse flies in sleeping sickness, though the proof of a developmental cycle in the fly was not made until 1909, by Kleine. The year 1898 brought two more important discoveries, — Ross's epoch-making proof of the transmission of malaria by mosquitoes, and Looss's discovery of infection by hookworm through the skin.

The relation of mosquitoes to yellow fever was discovered by the American Yellow Fever Commission in 1900, and to dengue by Graham in 1902; the relation of ticks to relapsing fever by Dutton and Todd, and independently by Koch, in 1905, and to spotted fever by Ricketts in 1906; the details of the transmission of plague by fleas by the British Plague Commission in 1905–1906, led up to by earlier experiments of others; the relation of lice to typhus by Nicolle and his colleagues in Algeria in 1909, and independently by Ricketts and Wilder and Anderson and Goldberger in Mexico in the same year; and the relation of *Triatoma* to South American trypanosomiasis by Chagas in 1909. In 1914 Miyairi and Suzuki followed out the life cycle of the Japanese schistosome, and the following year Leiper did the same for the Egyptian schistosomes; in 1914, also, Nakagawa incriminated crabs as the intermediate hosts of lung flukes. In 1916 Stewart discovered the migration through the heart and lungs of larvæ of Ascaris. In 1917 the life cycle of the broad tapeworm was completed by Rosen and Janicki. In 1918 Muto completed the life cycle of *Clonorchis*, important parts having previously been contributed by Kobayashi. In 1921 Nakagawa elucidated the life cycle of *Fasciolopsis*. In 1918 to 1920 Darling called attention to the importance of quantitative data in hookworm infections, which revolutionized methods of hookworm study and control, and from 1921 to 1926 important contributions were made to the epidemiology of hookworm by Cort and his colleagues and by the writer. In 1921 the Sergents and their colleagues experimentally produced an oriental sore by inoculating an infected sandfly, *Phlebotomus papatasi*, into the skin, and in 1924 Knowles, Napier and Smith showed the readiness with which the parasite of kala-azar develops in another sandfly, *P. argentipes*, and Shortt, Barraud and Craighead, in 1926, worked out the details of the development. In 1926 Blacklock proved a blackfly to be the transmitter of the filarial worm *Onchocerca* and in 1927 Sharp proved *Culicoides* to be transmitters of another filarial worm, *Acanthocheilonema perstans*.

Treatment has likewise developed at a rapid rate. Whereas little progress has been made with drug treatment of most bacterial diseases, and much has been done since Pasteur's time with active and passive immunization, the opposite is true in the case of animal parasites. In the field of protozoölogy one of the earliest specific remedies was quinine, introduced into Europe in the 17th century; it held the field until a synthetic substitute, plasmochin, was introduced in 1926. Schaudinn, in 1910, produced salvarsan which, with its derivatives, stands as a specific for syphilis and other spirochætal diseases. In 1912 Rogers proved the value of emetin in amebic dysentery, although the drug from which it is prepared, ipecac, was recognized as valuable in the treatment of dysentery since its introduction to Europe from Brazil in the 17th century. In 1914 Vianna, in Brazil, discovered the value of tartar emetic for leishmaniasis.

Anthelmintics effective against tapeworms, such as male fern, cusso, and areca nut, have been known for centuries, and santonin as a drug for ascaris and oxyuris has long been known; concoctions of *Artemisia*, from which santonin is made, were used by the Greeks and Romans, and were familiar to natives of India and other countries centuries ago. About 1880 the value of thymol for hookworm infections was discovered by Bozzolo, Parona, and other Italian workers, and it held the field as a treatment for nematode infestations for over thirty years. In 1913 oil of chenopodium, previously tried but repudiated, was shown by Schüffner and Verwoort in Sumatra to be preferable to thymol; within two years it came into very extensive use, both for hookworm and ascaris. In 1921 Hall introduced carbon tetrachloride, and since that time many millions of cases have been treated with that drug; in 1925 Hall and Shillinger suggested tetrachlorethylene as a substitute, and it may eventually replace carbon tetrachloride. Meanwhile, in 1917–19, McDonagh, and independently Christopherson, discovered the value of tartar emetic against schistosomes. In 1927 Faust and Khaw showed that gentian violet and related dyes had a beneficial effect against *Clonorchis*.

Preventive measures, of course, depend on knowledge of the biology of the parasites involved, and have kept pace with the development of this knowledge. There are very few parasitic diseases which we do not now know how to control, but practical ways of applying the necessary control measures still occupy the attention of parasitologists in all parts of the world.

The discoveries mentioned in this brief résumé of the history of parasitic diseases are but a few of the more conspicuous milestones on the path of progress of modern medicine as related to animal parasites. They may be likened to the posts of a fence, while the hundreds of other discoveries, less striking in themselves, perhaps, but nevertheless necessary, correspond to the pickets. The posts are useless without the pickets as are the pickets without the posts. There is not one of the great outstanding discoveries in the field of parasitology and preventive medicine which could have been made without the aid of the less illustrious accomplishments of many other scientists. Our present ability to cope with and control disease is due not alone to the great work of such men as Manson, Laveran, Ross, Pasteur, Koch, Reed, Schaudinn and Ricketts, but also to the careful, painstaking work of thousands of other investigators, who, often without any semblance of the honor and recognition which they deserve, and perhaps even under the stigma of public denunciation, work for the joy of the working and feel amply repaid if they add a few pickets to the fence of scientific progress.

CHAPTER II

PARASITES IN GENERAL

The world of animal life consists of communities of organisms which live by eating each other. In a broad sense all animals are parasites, in that they are helpless without other organisms to produce food for them, on which they are therefore dependent. Plants alone are able to build up their body substance out of raw sunlight and chemicals. Herbivorous animals, when they feed on vegetation, exploit the energy of the plants for their own use. Carnivorous animals, in turn, exploit the energies of the herbivorous ones, larger carnivores exploit the smaller ones, etc., the whole series thus constituting what ecologists call a food chain; many such chains can be traced in any animal community. But animals and plants are not preyed upon alone by successively larger forms which overpower and eat them; they are also preyed upon by successively smaller forms which destroy only small, more or less replaceable portions, or even more subtly exploit the energies of the host by subsisting on the food which the host has collected with great expenditure of time and energy. Elton (1927) says "The difference between a carnivore and a parasite is simply the difference between living upon capital and income, — between the burglar and the blackmailer. The general result is the same although the methods employed are different." A man's relation to his beef cattle is essentially that of a tiger to its prey; his relation to his milk cattle and sugar maple trees is essentially that of tapeworms or hookworms to their hosts. There is every gradation between parasites and carnivores, *e.g.*, hookworms, leeches, horseflies, blood-sucking bats and tigers; there are also all gradations between parasites and saprophytes, or organisms which live on the wastes or left-overs, *e.g.*, *Endamœba histolytica*, feeding on the tissue of the host; *Trichomonas hominis*, feeding, in part at least, on digested foods which would otherwise be converted into tissues; *Endamœba coli*, feeding on still undigested particles and bacteria; and the coprozoic amebæ, feeding on the waste fecal matter of the host.

The popular notion that parasites are more morally oblique in their habits than other animals, as if they were taking some unfair and mean advantage of their hosts, is, as Elton remarks, unjustified. Carnivores and herbivores have no interest in the welfare of their prey, and ruthlessly destroy them; parasites, of necessity, cannot be so inconsiderate, for their welfare is intimately bound up with the welfare of the host. "A parasite's existence," says Elton, "is usually an elaborate compromise between extracting sufficient nourishment to maintain and propagate itself, and not impairing too much the vitality or reducing the numbers of its host, which is providing it with a home and a free ride." A dead host is seldom of any use to a parasite in its adult state, though it may capitalize the death of an intermediate host as a means of attaining its destination in the definitive host. Food of the right kind and in sufficient quantity is the burning question in all animal society; in the case of parasites this resolves itself into the question of what to do when the host dies; most internal parasites, as adults, are so specialized for a protected life in the body of the host that they are unable to take any steps to deal with this situation. The result is that they make no attempt to do so and resign themselves to dying with their hosts, leaving it to their offspring to find their way to another host in order to continue the race, and since the offspring have to run enormous risks in order to succeed, they have to be produced in correspondingly enormous numbers, running into millions. Since food is the hub of the wheel of animal life, it is natural to find that many parasites have taken advantage of the food habits of their hosts in order to propagate themselves from host to host. Intestinal protozoa, such as amebæ and flagellates, usually solve the problem by entering into a resistant cystic stage in which they can survive outside the body until they can re-enter a host with its food or water; blood protozoa, such as trypanosomes and malaria parasites, are adapted to living temporarily in blood-sucking insects which feed on the host and subsequently re-inject them into another host; most flukes and tapeworms lay eggs which develop in the bodies of animals which the host habitually eats, or which is eaten by a third animal which is then eaten by the definitive host; some intestinal nematodes, such as the spiruroids, do likewise; others, such as ascaris, follow the tactics of intestinal protozoa; and still others, such as hookworms, produce self-reliant embryos which actively burrow into the skin of their hosts; most parasitic arthropods are able to migrate from host to host when these come in contact with each other, directly or indirectly; but the blood-sucking flies, which anticipated airplane transportation, have no worries about this matter, and can go at will from host to host. The result of the dependence of parasites to such a large extent on the food habits of animals is that the food habits largely determine the nature of the parasites harbored. Ascaris, trichuris, intestinal protozoa, etc. are abundant where unsanitary conditions favor fecal contamination of food or water; many fluke infections of man are abundant in localities in the Far East where fish is habitually eaten raw; tæniæ are abundant where pork or beef is eaten raw or partly cooked; guinea-worms are common where infected Cyclops is ingested with drinking water; and spiruroid infections occur only accidentally in man because the human animal is nowhere habitually insectivorous in habit.

Parasitism, in the restricted sense of a small organism living on or in, and at the expense of, a larger one, probably arose soon after life began to differentiate in the world. It would be difficult, if not impossible, to explain step by step the details of the process of evolution by which some of the highly specialized parasites reached their present condition. In some cases parasitism has probably grown out of a harmless association of different kinds of organisms, one of the members of the association, by virtue, perhaps, of characteristics already possessed, developing the power of living at the expense of the other, and ultimately becoming more and more dependent upon it.

Kinds of Parasites. — There are all kinds and degrees of parasitism. There are facultative parasites which may be parasitic or free-living at will, and obligatory parasites which must live on or in some other organism during all or part of their lives, and which perish if prevented from doing so. There are intermittent parasites which visit and leave their hosts at intervals. Some, as mosquitoes, visit their hosts only long enough to get a meal, others, as certain lice, leave their hosts only for the purpose of moulting and laying eggs, and still others, as the cattle tick, *Boöphilus annulatus*, never leave except to lay eggs. There are parasites which pass only part of their life cycles as parasites; botflies, for instance, are parasitic only as larvæ, hookworms only as adults. Some organisms live parasitically in two or more different animals, often of widely different species, in the course of their life histories. Such, for instance, are the filarial worms and numerous protozoan parasites, which begin life in a vertebrate animal, continue it in an insect, and finish it in a vertebrate again; the tapeworms, which begin life in certain vertebrates and finish it in other individuals of the same or different species; the flukes, which begin life as free-living embryos, continue it through two or more asexual generations in particular species of snails, become again free-living or else parasitize second intermediate hosts such as crabs or fishes, and finally gain admittance to their ultimate vertebrate hosts. There are permanent parasites which live their whole lives, from the time of hatching to death, in a single host, but in which the eggs, or the corresponding cysts in the case of protozoa, must be transferred to a new host before a second generation can develop. Such are many intestinal protozoans and round worms. The final degree of parasitism is reached, perhaps, in those parasites which live not only their whole lives, but generation after generation, on a single host, becoming transferred from host to host only by direct contact. Such are the scab mites and many species of lice. There is every gradation among all the types of parasites mentioned above, and a complete classification of parasites according to mode of life would contain almost as many types as there are kinds of parasites.

It is sometimes convenient to classify parasites according to whether they are external or internal. External parasites, or ectoparasites, are those which live on the surface of the body of their hosts, sucking blood or feeding upon hair, feathers, skin or secretions of the skin. Internal parasites live inside the body, in the digestive tract or other cavities of the body, in the organs, in the blood, in the tissues, or even within the cells. No sharp line of demarcation can be drawn between external and internal parasites since inhabitants of the mouth and nasal cavities, and such worms and mites as burrow just under the surface of the skin, might be placed in either category.

Effects of Parasitism on Parasites. — The effect of parasitism is felt by both parasite and host. There is a sort of mutual adaptation between the two which is developed in proportion to the time that the relationship of host and parasite has existed. It is obviously to the disadvantage of internal parasites to cause the death of their host, for in so doing they destroy themselves. It is likewise to the disadvantage of external parasites, not so much to cause the death of their host, as to produce such pain or irritation as to lead to their own destruction at the hands of the irritated host. It is interesting to note, for instance, that insects which depend to a large extent on man for food have less painful bites than do insects which only occasionally or accidentally bite human beings. Together with a softening down of the effects of the parasite on the host, there is a concomitant increase in the tolerance of the host to the parasite. It is a well-established fact that a disease introduced into a place where it is not endemic, *i.e.*, does not normally exist, is more destructive than in places where it has long been present. In an abnormal host the delicate adjustment between host and parasite is missing and usually either the parasite fails to survive, or else the host is severely injured or destroyed; a high degree of pathogenicity of a parasite may be considered *prima facie* evidence of a recent and still imperfect development of the host-parasite relation. An organism and the parasites which are particularly adapted to live with it may, in a way, be looked upon as a sort of compound organism. Those parasites which live part of their lives in vertebrate animals and part in other parasites of these animals, as lice, ticks and biting flies, are absolutely dependent for their existence on the relationships of the vertebrates and their parasites, and form a sort of third party to the association.

Aside from the toning down of their effects on the host, parasites are often very highly modified in structure to meet the demands of their particular environment. As a group, parasites have little need for sense organs and seldom have them as highly developed as do related free-living animals. Fixed parasites do not need, and do not have, well-developed organs of locomotion, if, indeed, they possess any at all. Intestinal parasites do not need highly organized digestive tracts, and the tapeworms and spiny-headed worms have lost this portion of their anatomy completely. On the other hand, parasites must be specialized, often to a very high degree, to adhere to or to make their way about in their particular host, or the particular part of the host, in which they find suitable conditions for existence. Examples of specializations of external parasites are the compressed bodies of fleas, permitting them to glide readily between the hairs of their hosts; the backward-projecting spines of fleas, which are of much assistance in forcing a path through dense hair by preventing any back-sliding; the clasping talons on the claws of lice; the barbed proboscides of ticks; and the tactile hairs of mites. In these same parasites can be observed marked degenerations in the loss of eyes and other sense organs, absence of wings, and, in some cases, reduction of legs. Internal parasites are even more peculiar combinations of degeneration and specialization. They possess all sorts of hooks, barbs, suckers and boring apparatus, yet they have practically no sense organs or special organs of locomotion, a very simple nervous system, and sometimes, as said before, a complete absence of the digestive tube.

Still more remarkable are the specializations of parasites in their reproduction and life history, to insure, as far as possible, a safe transfer to new hosts for the succeeding generations. Every structure, every function, every instinct of many of these parasites is modified, to a certain extent, for the sole purpose of reproduction. A fluke does not eat to live, it eats only to reproduce. The inevitable death of the host is the parasite's dooms-day, against which it must prepare by producing all the offspring possible, in the hope that enough will survive to keep the race from extinction. The complexity to which the development of the reproductive systems may go is almost incredible. In some adult tapeworms not only does every segment bear complete male and female reproductive systems, but it bears *two* sets of each. The number of eggs produced by many parasitic worms may run well into the millions. The complexity of the life history is no less remarkable. Not only are free-living stages interposed, and intermediate hosts made to serve as transmitting agents, but often asexual multiplications, sometimes to the extent of several generations, are passed through during the course of these remarkable experiences.

Modes of Infection and Transmission. — The portals of entry and means of transmission of parasites is a question of the most vital importance from the standpoint of preventive medicine. In the past few decades wonderful strides in our knowledge along these lines have been made, but there is much yet to be found out.

Many parasites may be spread by direct or indirect contact with infected parts, *e.g.*, the spirochætes of syphilis and yaws, the mouth amebæ, itch mites and, of course, free-moving ectoparasites. The parasites of the digestive system and of other internal organs gain entrance in one of two ways. They may bore directly through the skin as larvæ, *e.g.*, hookworms. More commonly they enter the mouth as cysts or eggs, *e.g.*, dysentery amebæ and *Ascaris;* as larvæ, *e.g.*, tapeworms; or as adults, *e.g.*, leeches. Access to the mouth is gained in many different ways, but chiefly with impure water, with unwashed vegetables fertilized with " night soil," with food contaminated by dust, flies or unclean hands, or with the flesh of an animal which has served as an intermediate host. The parasites of the blood or lymphatic systems usually rely on biting arthropods (insects, ticks and mites) to transmit them from host to host, and it is in this capacity, *i.e.*, as transmitters and intermediate hosts of blood parasites, that parasitic arthropods are of such vast importance (see p. 379–380).

Geographic Distribution. — The distribution of parasites over the surface of the earth is dependent (1) on the presence of suitable hosts, and (2) on habits and environmental conditions which make possible the transfer from host to host. A human parasite which does not utilize an intermediate host is likely to be found in every inhabited region of the world, providing its particular requirements with respect to habits and environmental conditions are met, and if it can also live as a parasite in other animals it may occur even beyond the limits of human habitation. Parasites such as amebæ, intestinal flagellates, pinworms, and itch mites, which require only slight carelessness in habits for their transfer, and are largely independent of external conditions, are practically cosmopolitan, but vary in abundance with the extent of the carelessness on which their propagation depends. *Ascaris* and *Trichuris* are only slightly more limited since they require some time outside the body to reach the infective stage, and are susceptible to heat and dryness. Hookworms are more limited, since they have to brave the dangers of the outside world as free-living organisms, unprotected by resistant egg shells; therefore not only heat and dryness, but also such factors as cold and nature of the soil came into play. When an intermediate host is involved, distribution is more limited, for not only must both hosts be present together, but the relations between them must be such as to favor the transfer of the parasites from one to the other. Sleeping sickness never occurs outside the range of certain species of tsetse flies, malaria beyond the range of certain species of Anopheles, or spotted fever outside the range of *Dermacentor andersoni.* But usually the distribution of the parasites is not as great as the distribution of its necessary intermediate hosts. A guinea-worm not only requires both man and certain species of Cyclops, but it requires conditions under which the Cyclops can be reached by the embryos and under which the infected Cyclops can be ingested by man. Even in the presence of both man and mosquitoes, filaria may not thrive, since it must have atmospheric conditions which give it time to penetrate human skin, after a mosquito has landed it there, before it dries up, and it has little chance in a place where houses and porches have mosquito-proof screens. *Clonorchis* requires not only the simultaneous presence of man, certain snails, and certain fish but it also requires unsanitary conditions making possible the access of eggs to the snails, a free association of infected snails and fish, and an established habit of eating raw fish. Sometimes ability to infect other hosts than man may keep alive an infection even when human habits preclude the possibility of more than occasional or rare access to the human body. No doubt the broad tapeworm would soon die out in the Canadian lakes if it were not that dogs and wild carnivores serve as reservoir hosts.

With modern transportation facilities, as remarked in the previous chapter, the possibilities of extension of the range of parasites are inincreased. With more frequent experimentation, parasites may find new suitable intermediate hosts, and the required environmental conditions, in new places. Yellow fever has failed, during all the past centuries, to gain access to the Far East only because of the long sea journey which exceeds the incubation period of the disease, and makes it possible to discover cases of yellow fever and block them, or mosquitoes which might have fed on them, from entering. Today the danger is greater. Sometimes altered environmental conditions cause some diseases to disappear and others to come. Thus malaria disappears with adequate drainage and typhus with cleanliness. On the other hand, Rhodesian sleeping sickness is the direct outcome of the civilization of East Africa, and the creation of conditions under which *Glossina morsitans* more frequently bites man and less frequently the diminishing wild game.

Resistance and Immunity. — Immunity or resistance to animal parasites is a question which has been the subject of much experiment and speculation in recent years. Until recently most of the work on immunity to disease has been done in connection with bacteria. It has been known for centuries that after a man or animal had recovered from certain diseases he, or it, was thereafter immune to that disease; for ages the Chinese have practiced inoculation of their children from mild smallpox cases rather than risk their exposure during destructive epidemics. Pasteur, in the last half of the 19th century, put the matter on a more scientific basis, and in the half-century since then there has grown up the science of immunology. It is worth noting, however, that although we know a great deal about the changes which bacterial infections induce in the nature and behavior of the blood, we are still almost as much at sea as ever as to *how* the changes are brought about. A number of ingenious theories have been advanced by Ehrlich, Bordet, Metchnikoff, Manwaring and others, but none of them have satisfactorily explained all the facts. We know that the presence of foreign proteins or antigens in the body result in ability of the blood, under certain circumstances, to dissolve them if they are not already in solution; to cause them to clump or agglutinate if in discrete particles; to precipitate them as solid particles if they are in solution; to " fix " oı use up a constituent of the blood known as complement, necessary for the dissolution of cellular antigens, but occuring whenever an antigen and antibody combine; and to stimulate the leucocytes to a heightened appetite for them and to increase their digestibility for the leucocytes. We also know that under certain circumstances the body is rendered immune to injury by them, while in other circumstances it is rendered highly susceptible to them when it was unharmed by them before — a condition known as anaphylaxis. We also know that when an animal is in a state of hypersusceptibility to a particular protein, injection of that protein into the skin causes a characteristic skin reaction; such skin reactions occur after injection of tuberculin into a person or animal infected with tuberculosis, of pollen extracts into the skin of hay fever patients susceptible to that particular pollen, or of extracts of foods into the skin of individuals with idiosyncrasies for them. All of these altered reactions are with few exceptions highly specific and are strongly elicited only by the particular protein involved. The blood of an animal injected with typhoid bacteria, for instance, will not react except in very mild degree to such closely related proteins as paratyphoid bacteria. But how all this is brought about is still almost as much a mystery now as it ever was, and we are almost as much in the dark as to the relation, if any, of these various " immune reactions " to actual immunity.

Naturally, since animal parasites as well as bacteria are made up of proteins, they too can bring about these various changed reactions, whenever their proteins actually get access to the blood. The blood and skin reactions mentioned above are of common occurrence and are in some instances of value in diagnosis. Thus, infection with the hydatid cysts of *Echinococcus* can be diagnosed by fixation of complement, by a precipitin reaction, or by a skin test, using fluid from a hydatid cyst as an antigen. Similar results are obtained with antigens prepared from schistosomes, trichina, lung flukes, etc., and probably can be obtained with any worms which actually live in the blood or tissues, but worms living in the alimentary canal or bile ducts (*e.g.*, *Ascaris*, hookworm, *Clonorchis*) give very uncertain and unreliable results. *Strongyloides*, however, burrowing into the walls of the digestive tract, is said to react well. In some protozoan infections similar reactions occur, and also some other ones. Thus spirochætes and trypanosomes are agglutinated by serum immune to them; in the case of the trypanosomes the process is distinguished by the term " agglomeration," since the parasites do not clump together in a haphazard manner but form rosettes, all attached centrally by their posterior ends, their free flagella pointing outwards (see Fig. 44). Blood immunized against either spirochætes or trypanosomes shows another peculiarity in that the blood platelets adhere to the parasites until the latter become laden with them; this phenomenon is called the " Rieckenberg reaction." Trypanosomes also acquire the property of attaching themselves to leucocytes, even dead ones, which undoubtedly aids in the process of phagocytosis, or the preying on invading organisms by leucocytes. While all of these " immune reactions" are of great theoretical interest, and often of value in diagnosis, their actual significance, if any, in resistance to infection is obscure.

Actual resistance or immunity in parasitic infections is a matter of paramount importance but little is yet known about it.

Natural immunity to particular infections is the birthright not only of species of animals, but also of races and even individuals; since natural immunity does not depend on previous contact with parasites, it is due largely to non-specific factors, such as mechanical obstruction, general phagocytosis, incidental parasiticidal properties of the the blood, and such factors as food temperature, etc. Neither natural nor acquired immunity is absolute, but both may be broken down by changes either in the host or in the parasite. Thus removal of the thyroid gland makes it easier to infect monkeys with kala-azar; and deficiency of vitamine A renders pigs susceptible to infection with the human *Ascaris*. Removal of the spleen in rats unleashes in full fury certain minute organisms of uncertain affinities, *Bartonella muris-ratti*, which were previously harbored in such small numbers as to have been unobserved, but subsequently cause a pernicious and often fatal anemia. Similar flaring up of latent infections with *Piroplasma* infections have been observed. Removal of the spleen also increases the virulence of trypanosome infections in rats, and it causes these animals, which usually recover from infections with *Treponema recurrentis*, to succumb regularly, with failure of production of " antibodies " which dissolve the spirochætes. Kritschewski and his students have also shown that removal of the spleen, and blockade of the " reticulo-endothelial " system, in some obscure way prevents the action on trypanosomes of injected drugs, ordinarily destructive to them, so that the drugs are practically harmless. On the other hand human beings, usually insusceptible to *Trypanosoma brucei* infections, become infected when the parasites have had an opportunity to accustom themselves to human blood in the guts of tsetse flies. Hibernating animals are sometimes immune when otherwise susceptible. It is an interesting fact that not all individuals of a species are equally susceptible; there are all gradations between instances where only an exceptional individual is resistant, as in the case of man and malaria, and instances where only exceptional individuals are susceptible, as in the case of man and *Ancylostoma braziliense*. Age is an important factor in natural immunity; young animals are almost always more susceptible to infection than old ones. In nature this might be the result of previous infections as well as mere age, but experiments with previously parasite-free animals show that age alone increases resistance. Ransom (1921) in experiments with gapeworms in chickens found that of chicks from 1 to 8 weeks old, 86 per cent became infected; from 9 to 20 weeks, 66 per cent became infected, and from 21 weeks to adult, 29 per cent became infected. Herrick (1926) got similar results with *Ascaridia* infections in chickens, and (1928) with hookworm infections in dogs. Pigs and man both become more resistant to *Ascaris* infections with increasing age, and this appears to be true in most helminthic infections. Sandground (1928), however, thinks that age resistance is usually associated with abnormal or imperfectly adapted hosts; any incompatibility between host and parasite appears to become intensified with age. It may be significant that most cases of human infections with " foreign " worms, belonging in other animals, are recorded in children.

Acquired resistance undoubtedly plays an important part in protozoan and metazoan infections as well as in bacterial ones. Such resistance, in the case of protozoa, usually takes the form of antagonism to the parasites, so that they are unable to make headway and produce heavy infections; in the case of worms it takes three different forms:

(1) resistance to invasion of the parasites, (2) resistance to successful maturing of the parasites after entry, and (3) resistance to injurious toxic effects.

It is a matter of common knowledge that protozoan infections, after an acute attack, usually go into a chronic state in which the parasites may be few and hard to find; such a chronic state is often punctuated by relapses, due to the parasites taking advantage of a temporary weakening in the defenses of the host, as the result of fatigue, malnutrition, other diseases, etc. During the chronic periods of infection, there is usually a marked resistance to superimposed infections, although these may occasionally be possible. Fresh chancres do not develop in people with latent syphilis; adults in highly malarial countries, having been infected with malaria almost since birth, cannot develop acute malaria; chronic " carriers " of the dysentery ameba are not subject to amebic dysentery, etc. Taliaferro (1926) has analyzed some of the factors involved in resistance to trypanosome and malaria infections. Two quite distinct types of resistance appear, one the property of killing and dissolving the parasites, the other the property of inhibiting their reproduction. When a rat is infected with *T. lewisi*, the trypanosomes at first multiply, steadily and rapidly. Gradually the rat's blood acquires the property of inhibiting reproduction which becomes absolute by about the tenth day. About this time the blood develops another property and suddenly destroys a high percentage of the trypanosomes present, but a few, as in the similar case of relapsing fever spirochætes, physiologically alter themselves so that they are unaffected. Since, however, they cannot reproduce, the numbers never increase to produce a relapse. Eventually a second trypanocidal substance is produced which wipes out the majority, and usually all, of the parasites left and the rat is thereafter uninfected and immune. The permanent immunity of rats after one infection has run its course is due to the persistence of the reproduction-inhibiting property of the blood. If a few trypanosomes are inoculated by a flea, no demonstrable infection results because the parasites are unable to multiply. Some animals, notably the guinea pig, do not seem to have this fortunate power to control trypanosomes by stopping their reproduction, but they do produce the trypanocidal substances. When a guinea pig is infected with a " pathogenic " trypanosome, the latter multiplies until it is very numerous in the blood. Then suddenly the trypanocidal property comes into play and most of them are wiped out. But the few remaining ones, being unchecked in their reproduction, soon produce vast numbers again, thus bringing about a relapse, until a second trypanocidal property, active against the relapse strain, again reduces them. This relapsing process goes on until finally the parasites are either all killed or the guinea pig doesn't bring its defensive mechanism into play soon enough, and dies with myriads of trypanosomes in its blood. A precisely similar process occurs in infections with relapsing fever spirochætes (see p. 52). One might liken the process to the destruction of a regiment of soldiers by a poison gas, a few escaping by being able to apply gas masks protective against that particular gas. The regiment is then brought up to full strength with men all provided with such masks. The second crisis is comparable to attack by a second and different gas, from which a few escape by donning other gas masks protective against these new fumes, etc.

Mice seem to have no power of their own either to inhibit reproduction or to kill the trypanosomes, so the latter steadily multiply until the mice die. Strangely enough, however, if mice are treated with drugs in sufficient dose to kill most but not all of the trypanosomes, the drug in some way aids the body to develop a trypanocidal antibody, so that the animal is immune for some 20 days to the original " passage strain " of trypanosomes. The surviving ones, however, are immunologically altered just as they are after a crisis in guinea pigs, and bring about a relapse. Ritz (1914) partially cured a mouse 20 times with the production of 17 immunologically different strains. In different mice these do not recur in the same sequence, and an earlier strain might reappear subsequently.

Taliaferro and Johnson (1926) have found that a peculiar relation exists between the number of trypanosomes and the trypanocidal effectiveness of an immune serum in different quantities. With small numbers of parasites, any dose above a certain minimum one destroys the trypanosomes; with moderate numbers of parasites there are zones of effectiveness, so that doses four or ten times the minimum might have no effect, while one six times the minimum is again effective; while with very large numbers of parasites the serum is ineffective in any dose.

In malaria infections there is no reproduction-inhibiting mechanism present, yet the parasites are soon largely destroyed by a crisis, and are thereafter few in number. The basis for this destruction seems to lie in phagocytosis by the reticulo-endothelial system.

In metazoan parasites, as noted above, three different types of immunity come into play. In the first place there is evidence of resistance to invasion by forms which enter through the skin, such as hookworms and *Strongyloides*. This is probably purely physical and is related to race and age, and apparently not to immunity acquired as the result of previous infections. Resistance to the growth to maturity of parasites, however, unquestionably does result from earlier invasions. Fujinami (1916) tried to infect three horses with schistosomes. One animal which had been infected two years before and cured failed to acquire any worms at all, while two uninfected control animals had 10,000 and 20,000 worms respectively. Blacklock and Gordon (1927) showed that in experimental infections with the skin maggot, *Cordylobia anthropophaga*, in guinea pigs a high percentage of the maggots which entered the skin died, the majority of them within 20 to 40 hours. This immunity they showed to be present not in the blood but in the skin, and to be local, *i.e.*, a guinea pig with an immunized back could for a time still be infected in the abdomen, though gradually the maggot-killing property of the skin spread over greater areas. Immune skin grafted on a non-immune animal retained its power to destroy the maggots, and even spread its strange power to neighboring parts of the skin of the animal on which it was grafted, but pieces of immune skin removed from the animal, and no longer living, did not have the same deadly effect. It was furthermore observed that when immune skin was penetrated by maggots, a violent skin reaction occurred which did not appear on the occasion of original penetration. Such local immunity and reaction is not unique, — it is known to occur with many kinds of proteins. In the case of intestinal worms which attack the mucous membranes of the intestine it is conceivable that a similar local immunity might develop. Sandground (1928) found that dogs infected with *Strongyloides stercoralis* develop a high resistance to superinfections, whether cured or not, and cats even more. This immunity evidently pertained to the intestine, for in immune dogs the larvæ entered the skin and passed through the blood and lungs to the trachea as readily as in non-immune dogs; yet failed to mature. He, too, found that the blood itself did not contain the parasiticidal property. Sandground himself, as the result of a light and brief *Strongyloides* infection, apparently remained immune for at least 14 months, but at the end of 23 months he acquired an accidental infection which was still present a year later. Fulleborn (1921) found that dogs that had been heavily infected with larvae of ascarids (*Toxocara*) before birth were strongly resistant to later experimental infections, and later (1926) he found dogs to be highly resistant to superimposed infections with hookworms (*Uncinaria*) as long as worms were still present in the intestine. Sawyer (1925) has suggested that the equilibrium reached in hookworm-infested countries, whereby infections cease to increase with age, may be due to a similar mechanism, and the same explanation might be applicable to the decreasing rate of reinfection after treatment of hookworm infections. Stoll (1928) has observed that sheep infected with stomach worms (*Hæmonchus*) although exposed to constant reinfection, after a time begin to have fewer instead of more numerous worms.

In this connection the increase in percentage of eosinophile leucocytes in the blood, which is highly characteristic of nearly all worm infections, is of interest. Hadwen (1925) concluded from investigations on ascaris and warble infections in horses that the eosinophiles not only were concerned with the neutralization of poisonous products of the worms which made their way into the blood, but also secreted substances which were injurious to the worms themselves. Blacklock and Gordon found no evidence for this in their *Cordylobia* work, nor did Sandground in his *Strongyloides* work. In hookworm infections eosinophilia is nearly always present, and the injured mucous membranes are often heavily infiltrated with these cells, but the eosinophilia is not proportional to the degree of the infection. In severe clinical cases it is often notably low, and it may possibly be that the failure to produce eosinophiles to neutralize the worm toxins is the cause of the severity of the infections.

This brings us to the final phase of immunity — resistance to injurious effects of worm parasites. It is a well-known fact that one individual may suffer severely from a few dozen hookworms while another can harbor thousands with no evident ill effects, and this is probably true of all worm infections. Fulleborn *et al.* (1928) found that in Argentina the rate of loss of hemoglobin is by no means proportional to the number of worms harbored. A slight lowering of hemoglobin results from a moderate infection, and is not increased by infections twice as great; other workers have made similar observations. This type of immunity consists in ability to neutralize toxic products absorbed from the worms, and in the power to regenerate injured parts. Many contributing factors which favor this power are known. Nutrition is of prime importance, and the vitamine content of the diet is also involved; poorly nourished individuals suffer far more than others. The recent observation that the severe anemia caused by infection with the broad tapeworm disappears when a half-pound of liver is eaten daily, or a diet rich in liver extract and vitamines is partaken of, is very significant. Smillie's observations in Brazil on the relative harmlessness of heavy hookworm infections in individuals who drank plenty of milk is also significant. Other factors, such as fatigue, exposure, excesses of various kinds, disease, etc., are also important, just as they are in resistance to other kinds of infections. The proper functioning of the glands of internal secretion also plays a part; animals which have their thyroid glands removed are especially susceptible to infection, and the adrenal glands also come into the picture. Very likely the spleen also plays a part, as it does in some protozoan infections.

Host Specificity

Intimately bound up with the question of resistance of hosts, and the mutual adaptation of host and parasite to each other, is the question of limitation of parasites to particular hosts. In order for a parasite to live habitually in a host two conditions must be met: (1) a dependable means of transfer from individual to individual, and (2) ability to thrive in the individual when it gets there. It is the interplay of these two factors which determine in what hosts a parasite lives. Every parasite, of course, has at least one species of host, and sometimes several, in which these conditions are satisfactorily met, otherwise it would cease to exist. Usually there are other hosts in which one or both conditions are only occasionally met, in which case " accidental " parasitism results. Lack of a dependable means of transfer relieves man, for example, from all parasitic infections in which the parasites encyst in the bodies of insects and wait for their insect hosts to be eaten in order to reach the definitive host, since no race of man is habitually insectivorous. If it were not for this there is little reason to doubt but that there could be numbered among the common human parasites such species as *Hymenolepis diminuta, Dipylidium caninum, Gongylonema, Physaloptera,* various spiny-headed worms, etc. Since man is *not* habitually insectivorous these are more or less rare human parasites. On the other hand man must commonly be exposed to infection with such parasites as bird malaria, animal schistosomes, dog and cat hookworms, bird filariæ, etc., yet infection rarely or never occurs, because the parasites do not find suitable conditions for development in the human body. Such animals as rats, dogs, cats, and various domestic animals must very often be exposed to infection with human parasites, yet they habitually harbor very few of them. The conditions in the body of one species of animal are never exactly the same as in another species — they vary in the nature of the digestive fluids, food, bacterial content of the intestine, hydrogen ion concentration, temperature, and the more delicate and less easily observed factors concerned with reaction against the invaders and ability to overpower them. A parasite in its proper host has adapted itself to the particular set of conditions existing there, just as an insect or bird or plant has adapted itself to particular environmental conditions in its ecological " niche " in nature. Sometimes very slight modifications in an abnormal host make possible the survival of a " foreign " parasite. Cats, for example, would undoubtedly be common hosts of *Endamœba histolytica* if food did not pass through the digestive tract so fast that the cysts do not have time to hatch and the young amebæ to apply themselves to the intestinal wall. If an operation is performed to stop the movement of the intestinal contents for even a few hours, infection of cats with this parasite is easy. Even then, however, the ameba could not thrive in cats alone, for the stimulus which causes them to form cysts, by means of which they are spread from host to host, appears to be lacking. Many parasites perform migrations in the bodies of their hosts by which they ultimately reach their proper destination. They are so adjusted to their normal hosts that they are guided by a series of influences or stimuli which lead them in the right direction, and they only occasionally get lost. In strange hosts these road signs are misleading or missing, and the parasites become aimless wanderers in abnormal situations, unable to find their way to the localities in the body where they can successfully mature. Human hookworms, for instance, are guided by some condition in a human being to enter lymph or blood vessels in the skin, and so eventually reach the lungs and then the intestine; *Ancylostoma braziliense* does likewise in its normal hosts but usually fails in man, and rambles in the skin, causing creeping eruption. *Gastrophilus*, the bots of horses, find their way to the digestive tract of horses, but in man the guiding influences are missing and they creep about under the skin. Gnathostomes and *Lagocheilascaris* are other worms which lose their way in the human host and end up in subcutaneous cysts, where they have no business.

All animals tend gradually to extend their range by adapting themselves to slightly different conditions; free-living animals continually try to occupy new territories which differ in climate, vegetation or physical conditions from that to which they were accustomed, and parasites likewise attempt to utilize new hosts. But parasites are at a disadvantage compared with free-living animals; the latter are nearly always able to find intergrading conditions between two different types of habitat, whereas parasites cannot spread in this gradual manner; if they extend their range to a new host they must make the change in a single jump, for there is no middle ground where conditions are transitional. A song sparrow can find an infinite number of intergrading conditions between the damp, cool forests of the northwest and the dry, hot deserts of the southwest, but an ascaris can find no intergrading conditions between those found in the body of a pig and those in a human being. The comparison is nearer if we imagine an archipelago of islands each of which differs in climate, food resources and geological formations, and think of a particular species of animal adapted to life on one island attempting to colonize others. In some it would find the climate unfavorable, in others its accustomed food would be missing, in others it would have destructive enemies to contend with, and in others the types of shelter provided would be inadequate. The result would be that on some islands the animal would fail to establish itself at all; on others it would succumb after a temporary colonization; and on others the conditions might be such that the animal could survive long enough to readjust itself to the altered conditions, thus eventually giving rise to a new race or species which might in time have as much or more difficulty in living on the island of its ancestors as did its ancestors on the new island. These are essentially the conditions which parasites have to meet. In the case of free-living animals we have geographical subspecies or varieties; in the case of parasites we have hostal races. When these varieties become distinct enough so that they can be morphologically distinguished, and especially if they become so well adapted to a particular environment that they are not easily transferred to others, and do not merge with other races, they should rightly be regarded as species. If, however, they have only average differences or none at all, even though they may after a few generations thrive better in one environment than another, it seems more reasonable to regard them as races than as species, in the case of parasites as well as free living animals. Some parasitologists are inclined to consider extremely closely related parasites in different hosts as distinct species, to which separate species names are applied, until proved otherwise, whereas some tend to lump them all together. Such difficulties arise in all groups of parasites, — protozoa, worms and arthropods. The mere fact that one form of parasite is more readily transferred from one individual to another of a single host species, than from species to species, does not seem to be sufficient basis for regarding them as distinct species. Steiner has pointed out that certain soil nematodes, in the course of one or two seasons, involving in this case a considerable number of generations, may thrive far better on a particular host plant than on others, and show a very decided preference, yet such adapted forms can be readapted to other host plants, and there is no question as to their specific identity. A similar condition appears to exist in such parasites as itch mites, hookworms, *Ascaris*, *Hymenolepis*, *Trichomonas*, and many others. It has long been the custom of botanists and zoölogists to recognize geographic races by subspecific or varietal names, and it would seem advisable for parasitologists to recognize hostal races, where morphological differences are slight or absent, and where interchanges are even occasionally possible, by similar varietal names.

The Names of Parasites

In all branches of natural history it has been found not only expedient but necessary to employ scientific names, for there are estimated to be more than 10,000,000 species of animals. Common names, like nicknames, vary from place to place, and often the same name is applied to quite different organisms in different places. Linnæus in the 18th century devised a system of " binomial names " which consisted of the genus name beginning with a capital letter followed by a species name, in zoölogy beginning with a small letter, and both latinized in form, since latin came nearer being a universal language than any other. Strictly, the genus and species name is followed by the name of the man who first gave the species name, in parenthesis if the genus name is not the one he originally used, but in ordinary references to species this is omitted. The genus name may be likened to a sirname and the species name to a given name, *e.g.*, *Ascaris lumbricoides* is comparable with Smith, John. In order to avoid confusion there were adopted (in 1904) rules of nomenclature, known as the " International Code of Zoölogical Nomenclature," which make it impossible for any two animals to have the same name, or for the same name to belong to any two animals. A genus name can apply to only one genus in the entire Animal Kingdom, and a species name to only one species within a genus. The 10th edition of Linnæus' "Systema Naturæ" is accepted as the starting point for the names, no name proposed prior to that time having any standing. The first valid name given an animal is considered the correct one. Of course, if an animal is put in the wrong genus, it must be transferred to the right one. If a genus is split up, the animal may have to be placed in a new genus, for example, the old genus *Oxyuris* has been split into a number of genera. The oxyuris of the horse was the earliest one placed in the genus, therefore the *restricted* genus *Oxyuris* must contain this species and any others which fall into its subdivision of the old genus; since the human oxyuris falls into a different subdivision it comes out with the next available genus name, *Enterobius*. For the same reasons *Filaria bancrofti* is now *Wuchereria bancrofti*, etc. If two genera are combined, the oldest genus name applies to all the members of the merged genera. If the same animal is given different species names by different workers, the earliest name applies.

Although this system was established to prevent confusion, in many instances strict application of the rules has resulted in just the opposite. The number of possible errors and misinterpretations are disheartening, in consequence of which names, long recognized and accepted, have to be discarded for others, because some one shows that the established name was really first applied to another species, or an earlier name was overlooked, or for some other reason. Unfortunately the commoner animals are the ones which suffer most, for they are the most likely to have been redescribed by various workers and to have been shifted about from genus to genus. Unfortunate as this situation is, it is better than having no rules at all, and steps are now being taken to make names which have been in common usage for many years inviolable. The synonymy, or list of "aliases," of some of our common parasites is already deplorably long. In some instances there is a difference of opinion as to what the correct name should be.

Although the scientific names are sometimes barbarously long and at first may be very annoying and even terrifying, every student of parasitology, as of every other branch of biology, must overcome any childish aversion he may have for them, and become used to accepting and using them. They are not obstacles to be avoided, but valuable tools without which there would be hopeless confusion.

PART I — PROTOZOA

CHAPTER III

INTRODUCTION TO PROTOZOA

Place of Protozoa in the Animal Kingdom. — It is usual for zoölogists at the present time to divide the entire Animal Kingdom into two great sub-kingdoms, the Protozoa and the Metazoa. These groups are very unequal as regards number of species. The metazoa include all the animals with which the majority of people are familiar, from the simple sponges and jellyfishes, through the worms, molluscs, and the vast horde of insects and their allies, to the highly organized vertebrate animals, including man himself. The protozoa, on the other hand, include only microscopic or almost microscopic animals, the very existence of which is absolutely unknown to the average lay person. Although some protozoa are readily visible to the naked eye there are others which approach the limit of visibility under the highest magnifications of modern microscopes, and it is possible that some of the disease viruses, such as those causing yellow fever, dengue and papatasi fever, which have so far escaped detection, and are usually classed as filterable viruses, belong with the protozoa rather than the bacteria. There is no question but that in point of numbers of individuals the protozoa exceed the other animals, millions to one; a pint jar of stagnant water may contain many millions of these minute animals. About 10,000 species of protozoa have been described, but it is probable that there are thousands more which are not yet known to science.

The distinction between the protozoa and metazoa is based on a characteristic which is of the most fundamental nature The protozoa are animals which perform all the essential functions of life within the compass of a single cell. The metazoa, on the other hand, are many-celled animals, with specialized cells set apart to perform particular functions. A protozoan cell, even though sometimes living in a colony of individuals which are all bound together, can live its life and reproduce its kind quite independently of any other cells, having in itself the powers of digestion, respiration, excretion and secretion, sensibility, motility and reproduction. Most metazoan cells, on the other hand, are so specialized for particular functions that, if separated from the other cells with which they are associated in the body, they die almost immediately. It is customary to speak of protozoa as unicellular animals as contrasted with multicellular ones, but the term unicellular implies comparison of a protozoan with a single cell in a metazoan, whereas in reality a protozoan is comparable with an entire metazoan animal, and is therefore more correctly designated as a non-cellular than as a unicellular organism.

The very fact of evolution makes it difficult to draw a sharp and fast line between two groups of organisms, even between such fundamentally different groups as the protozoa and metazoa. There are always border line exceptions which make the work of the systematic zoölogist at once difficult and interesting. In the case in hand there are colonial protozoa in which all of the cells are not exactly alike, but have at least the beginnings of specialization. On the other hand, in the lowest metazoans, the sponges, there is only very limited specialization of the cells, while in the little-known animals which are designated as "Mesozoa" there is even less differentiation.

The distinction between protozoa and bacteria, though involving the distinction between animals and plants, is much more difficult. As we descend the evolutionary scale of plants and animals the usual distinctions between them disappear and it becomes difficult if not impossible definitely to place certain species in either the plant or animal kingdom. The possession of a distinct nucleus of some kind and some type of sexual reproduction are the characteristics which usually distinguish the protozoa from the less highly organized bacteria. Often, however, it is difficult to discover sexual phenomena, or to interpret them with safety, and the presence or absence of a nucleus is sometimes equally difficult to determine. In such cases peculiarities in life cycle, chemical reactions, staining properties and the like are resorted to as distinguishing characteristics. Most biologists are now inclined to group all of the single-celled animals and plants, including bacteria, into one great group known as the Protista, a suggestion first made by Ernest Haeckel. The existence of such groups of organisms as the spirochætes and the rickettsias, occupying intermediate positions between protozoa and bacteria, and of such groups as the chlorophyll-bearing flagellates, occupying an intermediate position between protozoans and green algæ, makes such a group as the Protista appear both natural and convenient.

Structure. — A protozoan, in its simplest form, conforms to the usual definition of a cell — a bit of protoplasm containing a nucleus. The nucleus varies greatly in different protozoa. Typically it is bounded by a nuclear membrane and has a fine network of radially arranged fibers composed of a substance known as linin; the chromatin, which is the most essential nuclear substance, and which somehow determines hereditary characteristics, is usually distributed either on the inner surface of the nuclear membrane or on the strands of linin. In most cases there is a body, the karyosome, usually central in position, which is composed for the most part of a substance called plastin; many protozoölogists think that it also contains chromatin, but the chromosomes appear to be formed mainly if not entirely from chromatin granules outside of the karyosome. The nucleus of some protozoa, *e.g.*, trypanosomes, has a very large karyosome, with a clear space between it and the periphery, while in other cases, *e.g.*, *Endamœba histolytica*, the karyosome is very small and inconspicuous, and the chromatin is distributed in granules encrusted on the nuclear membrane. The nature of the karyosome and distribution of the chromatin is sometimes of much value in identification, especially in the amebæ. Many protozoan nuclei contain a minute body, often imbedded in the karyosome, called a centriole, which seems to function as a centrosome. In some protozoa, *e.g.*, *Endamœba*, at the time of mitosis the centriole divides into two, which separate and take positions at the opposite ends of the spindle which subsequently forms, but the two centrioles remain connected by a deep-staining fiber which is called an intradesmose (Fig. 2). It is not universally agreed that the centrioles are actually homologous with centrosomes, since unquestionably true centrosomes occur outside the nucleus in some protozoa. In the ciliates the nucleus divides, after sexual reproduction, into two functionally distinct parts. The smaller micro-

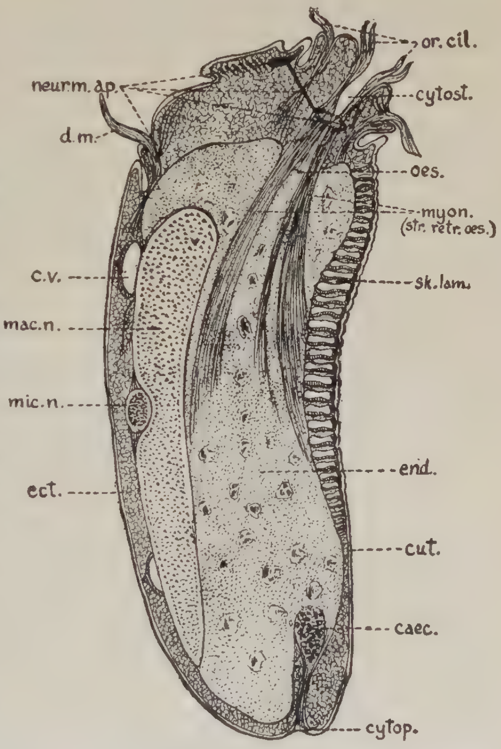

FIG. 1. A complex ciliate, *Diplodinium ecaudatum*, showing highly developed organelles; *cœc.*, cecum or rectal canal; *cut.*, cuticle; *c.v.*, contractile vacuole; *cytop.*, cytopyge or cell anus; *cytost.*, cytostome or cell mouth; *d.m.*, dorsal membranelle; *ect.*, ectoplasm; *end.*, endoplasm; *mac. n.*, macronucleus; *mic. n.*, micronucleus; *myon.* (*str. retr. es.*), myonemes, strands for retracting esophagus; *œs.*, esophagus; *or. cil.*, oral cilia; *sk. lam.*, skeletal laminæ. × 750. (After Sharpe.)

nucleus (Fig. 1, *mic.n.*) is concerned only with reproduction; it contains a karyosome, and divides by mitosis; the larger macronucleus (Fig. 1, *mac.n.*), on the other hand, though it arises originally from a micronucleus, becomes greatly modified both in form and function. It has chromatin, or at least chromatin-like material, in the form of numerous scattered granules; it divides by amitosis; and it disintegrates at the time of sexual reproduction. In some protozoa there is no nucleus as such, though the essential substance of the nucleus, chromatin, is always present, but in scattered particles. This is the condition which exists in such organisms as bacteria and spirochætes.

The cytoplasm of a protozoan is usually more or less clearly divisible into an outer and inner zone, the ectoplasm and endoplasm, respectively (Fig. 1). There is no fundamental difference between these two layers of protoplasm, merely a difference in density. The ectoplasm is the less fluid and comparatively clear, while the endoplasm is more fluid and somewhat granular. The clearness of the differentiation between ectoplasm and endoplasm is sometimes useful in distinguishing species of protozoans, especially amebæ. The ectoplasm differs from the endoplasm in function as well as in appearance. The ectoplasm may be likened to the body wall and appendages of higher animals while the endoplasm may be compared with the viscera or internal organs. The endoplasm digests food and has the power of secretion and excretion, while the ectoplasm produces the various organelles for locomotion, food getting, oxygen absorption and special senses. The term "organelle" is used in place of "organ" for structures which are only parts of a single cell. Whether or not protozoa have a definite shape depends on the presence or absence of a limiting membrane or cuticle. Amebæ have no outer membrane, and so, when relaxed in a fluid medium, they assume a spherical shape, which is modified in living forms by contractions, contacts, etc. Many

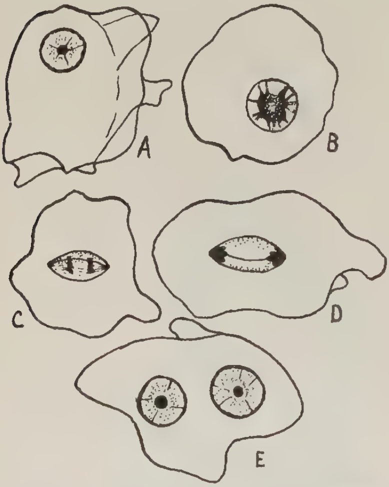

Fig. 2. Stages in mitosis of *Endamœba histolytica*. *A*, resting nucleus; *B*, prophase, with peripheral chromatin in strands (chromosomes ?), some of them split; *C*, early anaphase, with distinct intradesmose joining centrioles at poles; *D*, late anaphase, with distinct intradesmose; *E*, binucleate ameba resulting from mitosis. × 1500. (Sketched from figures by Kofoid and Swezy.)

forms have fine pellicles which allow change of shape but maintain a definite form other than the spherical one when the animal is relaxed, while in others the limiting membrane is so tough that the shape of the body is practically constant.

Organelles. — The organelles contained in a protozoan's body may be many and varied. Those connected with movement or locomotion differ in different groups. The simplest type of movement is by means of simple outflowings of the body cytoplasm known as pseudopodia (Fig. 3*A*). These are used both for locomotion and for the engulfing of food. In some species, *e.g.*, the amebæ, they are blunt, lobe-like projections of the body, but in others they are very slender and tapering; some are permanently supported by axial rods, in which case they are called axopodia (Fig. 3*B*). Pseudopodia are the characteristic organs of locomotion of the entire class Rhizopoda, to which the amebæ belong, but many flagellates and Sporozoa, *e.g.*, the malaria parasites, also have the power of ameboid movement by means of pseudopodia.

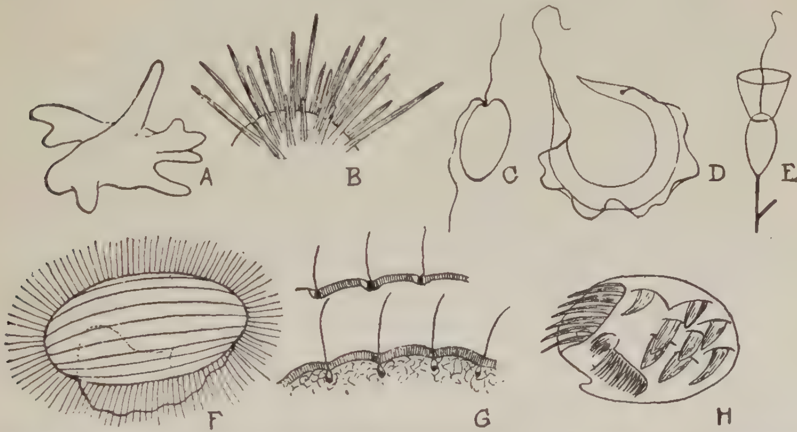

FIG. 3. Types of organs of locomotion in Protozoa; *A*, *Amœba* with pseudopodia; *B*, a heliozoan with "axopodia"; *C*, *Bodo* with free flagella; *D*, *Trypanosoma* with flagellum attached to undulating membrane; *E*, Choanoflagellate with flagellum and "collar"; *F*, *Pleuronema* with cilia and undulating membrane formed of fused cilia; *G*, modes of insertion of cilia; *H*, *Aspidisca* with cirri. (Figs. *F* to *H* from Calkins.)

Flagella and cilia are usually constant in arrangement and form. Flagella (Fig. 3*C*) are characteristic of the class Mastigophora, but they also occur in some stages in the life cycle of certain amebæ and in the sperm-like microgametes of Sporozoa. They are long whip-like outgrowths, capable of violent lashing or of rippling movements, and composed of a fine filament, the axoneme, surrounded by a thin film of cytoplasm. Except in one group of flagellates, the Hypermastigida, which are mostly parasites of white ants, and more or less intermediate between flagellates and ciliates, the flagella are only from one to eight in number. They may be directed forward or trail behind, or may be attached to the side of the body by a delicate undulating membrane (Fig. 3*D*); if more than one is present they may be all alike, and perform similar functions, or they may be widely different. A flagellum always arises from a minute deep-staining body called a basal granule or blepharoplast. There has been much difference of opinion as to the origin and functions of the blepharoplast, which cannot be adequately discussed here. In many parasitic flagellates there is another deep-staining body, called the parabasal, about the real nature of which there is also much dispute; it is especially well exemplified in the trypanosomes and related flagellates. In many other flagellates there are similarly-staining bodies which by some authors are considered as homologous to parabasals, and by others as totally distinct. In the flagellates which have typical parabasals these appear to be connected with the blepharoplasts by cone-shaped fibrous membranes, and sometimes to the nucleus by a fiber; these connecting structures are called rhizoplasts (Fig. 4). The blepharoplast and parabasal together constitute a body which is called a kinetoplast, the function of which seems to be the control and coördination of movement

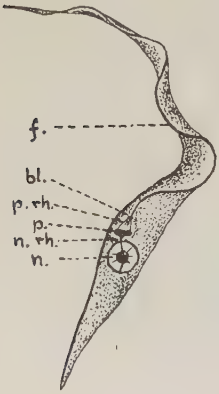

FIG. 4. *Trypanosoma cruzi*, showing kinetoplast and associated structures. *bl.*, blepharoplast; *f*, flagellum; *n*, nucleus; *n. rh.*, nuclear rhizoplast; *p.*, parabasal; *p. rh.*, parabasal rhizoplast. (After Chagas.)

As a result of a mistaken interpretation of the parabasal as a second, functionally distinct nucleus, analogous to the functionally distinct micronucleus of ciliates, but in this case concerned with movement rather than reproduction, certain German workers erected an Order Binucleata, and included in it the blood flagellates, certain other flagellates, and even the malaria parasites and related forms, in which they found granules which they regarded as the second nucleus. This classification is now of only historical interest.

Cilia (Fig. 3*F*), which are characteristic only of the Sub-phylum Ciliophora, have a structure similar to flagella, and like them arise from individual basal granules (Fig. 3*G*), but they are much shorter, more numerous, and beat rhythmically by a bending to one side. There is much more coördination of movement than in the case of flagella, and regular waves of beats of the cilia can be seen passing over the body of a ciliate. Sometimes rows of cilia are connected by a delicate cytoplasmic membrane into a " membranelle " (Fig. 3*F*), which functions somewhat like an undulating membrane, while in other cases, especially in creeping forms, brushes of cilia fuse together into stout organs called " cirri " (Fig. 3*H*).

Of quite a different nature, but none the less organelles of movement, are the myonemes (Fig. 1, *myon.*) found in many protozoa, and analogous to the muscle fibers of metazoa. They enable the animals to bend and twist their bodies. The myonemes are extremely delicate contractile fibers which run in various directions in the ectoplasm of the animal; they occur most commonly in flagellates and ciliates. In some flagellates and ciliates structures have been described, consisting of fibrils and minute deep-staining bodies, which have been interpreted as a more or less highly organized neuromotor apparatus, *i.e.*, a definitely arranged and organized substance having a nervous control over the myonemes and cilia or flagella (Fig. 1, *neur. m. ap.*).

Organelles for food-taking occur chiefly in the flagellates and ciliates. Such protozoans may have a " cytostome " or cell mouth for the ingestion of food (Fig. 1), and a " cytopyge " or cell anus for the elimination of waste matter. They may also have a delicate membranous pharynx (Fig. 1, *cytost.*) for leading the food material into the endoplasm, and food vacuoles into which the food is accumulated and in which it is circulated inside the body. In some protozoans, namely the Suctoria, a much modified group of ciliates, there are developed sucking tentacles for the absorption of food. In others there are tiny capsules in the ectoplasm, the trichocysts, containing minute threads which can be shot forth when stimulated, and used either to overpower prey or for protection from enemies. For the excretion of waste products of the body there is often present one or more contractile vacuoles (Fig. 1, *c.v.*), little cavities in the protoplasm of the body which expand with water containing urea and other waste matters conducted to them by tiny radiating canals, and which periodically contract, forcing their contents outside of the cell, sometimes through a definite excretory pore. Sense organs in the form of pigment spots sensitive to light, and outgrowths sensitive to chemical substances, giving, perhaps, a sensation comparable with taste, are present in some species, especially in free-living ones. Various organelles serving the function of a skeleton may be developed in the form of a tough cuticle, a chitinous, calcareous or siliceous shell, a chitinous supporting rod or " axostyle " (Fig. 26), or even a complicated internal skeleton of calcareous material. While no protozoan possesses all of these organelles, many possess a considerable number of them and exhibit a degree of complexity and organization almost incredible in a single-celled animal which is barely, if at all, visible to the naked eye.

Physiology and Reproduction. — In their physiology and manner of life the protozoa differ among themselves almost as much as do the metazoa. Some ingest solid food through a cytostome or by wrapping themselves around it, others possess chlorophyll and are nourished in a typical plant manner, and still others absorb nutriment by osmosis from the fluids or tissues in which they live. Acid substances corresponding to the gastric juice and alkaline substances simulating the intestinal juices may be present in the protozoan body, often localized in definite regions, and acting upon the food as it circulates in the food vacuoles. The waste material either is voided through a cytopyge or is left behind by a simple flowing away of the protoplasm. Body excretions are collected by the contractile vacuoles and voided by them, or they are simply passed through the body wall by osmosis.

The multiplication or reproduction of protozoans is of two quite distinct types, an asexual multiplication, more or less comparable with the multiplication of cells in a metazoan body, and sexual reproduction, comparable with a similar phenomenon in the higher animals. Several common asexual methods of multiplication occur amongst protozoans, namely, simple fission, or division into two more or less equal parts; budding, or separation of one or more small parts from the parent cell; and multiple fission or schizogony, a breaking up into a number of individuals or spores. In the flagellates simple fission begins at the anterior end of the body and proceeds backward, special structures, such as a cytostome or axonemes, being reduplicated before division. In the ciliates, on the other hand, division is transverse. Fission may occur either in free-living or encysted forms.

Schizogony is a form of multiplication, typical of the Sporozoa, in which the nucleus of the parent cell, the schizont, undergoes repeated division without corresponding cell divisions. When this process is completed the nuclei migrate to the periphery of the cytoplasm, where, surrounded by part of the cytoplasm, they bud off as daughter cells or merozoites, leaving some residual cytoplasm, pigment, etc., which disintegrates. After the sexual process a similar method of reproduction occurs, but its end products, called sporozoites, may be quite different from the merozoites, and the process is not repeated over and over again. To distinguish it from the asexual schizogony, this post-sexual multiplication is called sporogony. Sometimes the parent cells divide into a number of intermediate bodies, the agametoblasts in the asexual, and sporoblasts in the sexual cycle, which in turn give rise to the actual merozoites or sporozoites.

It is probable that in most if not all cases the nucleus divides by some form of mitosis, although the process is by no means as uniform as it is in the metazoa, and many different modifications of it occur. Although in some forms, *e.g.*, many amebæ, typical chromosomes are formed (Fig. 2), in other cases there is no evidence of this.

Multiplication by one of the asexual methods may go on with great vigor for a long time, but sooner or later some modification of the process occurs. In many protozoa a process in every way comparable to sexual reproduction in higher animals occurs. In the ciliates this takes place by conjugation, *i.e.*, a temporary union of two individuals during which time a daughter nucleus of one enters the other and fuses with its remaining nucleus, and vice versa; at the end of the process the two individuals separate, each being now a fertilized cell. In many other protozoa two individuals, which may be regarded as gametes, unite permanently and their nuclei fuse, a process which is known as copulation. In some cases the gametes are indistinguishable from ordinary asexually multiplying individuals, while in others the gametes are smaller cells produced by a special process of multiplication; in this case the parent cell is called a gametocyte. When there is no visible difference between the gametes, the process of fusion is called isogamy, whereas when the gametes differ in size, form, motility, etc., the process is called anisogamy, but there are all gradations between isogamy and a condition of anisogamy in which one gamete, the macrogamete, corresponds closely to an ovum, being large, immobile, and with a relatively large amount of cytoplasm charged with reserve food material, while the other, the microgamete, is relatively minute, is actively motile by means of flagella, and contains very little cytoplasm, being thus essentially similar to a spermatozoön.

While no process which can be interpreted as sexual reproduction has been observed in many protozoa, including the parasitic amebæ and hæmoflagellates, it is very likely that some process which accomplishes a similar rejuvenescence will eventually be discovered in all of them.

The analogy between a protozoan life cycle and a metazoan life cycle has become understood only in recent years. As a result of the painstaking experiments of Calkins and other protozoölogists, it is now usual to compare the entire life cycle of a protozoan animal from one sexual reproduction to the next, including all the intervening asexual generations, resulting perhaps in millions of individuals, with the life cycle of a single metazoan. According to this view the asexual reproduction, as remarked above, is comparable with the multiplication of cells in a metazoan body, except that, instead of all the cells resulting from such multiplication remaining together and becoming specialized for particular functions, they separate and live as independent individuals. Just as the cells of a metazoan body grow old after a variable length of time and lose their youthful vitality and reproductive power, so the protozoan cells, after a variable number of multiplications, gradually lose their vitality and reproductive power. In the metazoan certain cells have the power of renewing their waning vitality by union with a cell of the opposite sex (sexual reproduction), thus beginning the cycle again. In the protozoan the sexual phenomena which have been observed are believed to have the same significance, and there is evidence that at least in some protozoa the sexual power may be confined to certain individuals which would then be comparable with the sex cells of the metazoans. Calkins' experiments led him to believe that in *Paramecium,* a common ciliated protozoan on which he experimented particularly, old age and death were inevitable after a variable number of asexual generations without sexual reproduction. It has been discovered, however, that when conditions of life are perfect some ciliates may continue to multiply asexually for an indefinite time. In *Paramecium,* however, a complete reorganization of the cells occurs periodically which apparently has an effect similar to that produced by sexual reproduction, the animals having renewed vitality for many generations. This remarkable process, named "endomixis," is strikingly analogous to parthenogenesis (development of unfertilized eggs) in higher animals. Another analogy is that under unfavorable or adverse conditions sexual reproduction replaces endomixis, just as in such animals as rotifers and small crustaceans it replaces parthenogenesis, though either endomixis or parthenogenesis apparently may continue indefinitely with conditions favorable.

Another phenomenon which is often, though not always, associated with sexual reproduction is encystment, *i.e.*, the development of an impervious enclosing capsule in which the delicate protozoan cell is able to resist extremely adverse environmental conditions, such as unfavorably high or low temperatures, drouth, presence of injurious substances, lack of oxygen, etc. The degree of protection afforded by encystment can be judged from the fact that encysted amebæ exist in considerable numbers on the sun-baked sands of Egypt. Encystment may take place whenever environmental conditions become unfavorable, or as a normal stage of existence following sexual reproduction, thus being comparable with the impervious shelled eggs of many higher animals, or sometimes as a step preliminary to some form of asexual reproduction. The majority of parasitic protozoans which are not transmitted by an intermediate host adapt themselves for passive transfer from one host to another by encystment.

A full understanding of the significance and limitations of the sexual and asexual phases of the life histories of parasitic protozoa is of great importance, since means of control and prevention often hinge on these points. In many species of protozoan parasites a different host is required for the sexual portion of the life history than that utilized for asexual reproduction, though this is not true, in general, of the intestinal parasites. Some species, although normally utilizing a second host for a special cycle which is presumably sexual, are apparently able at times to pass from host to host without the intervention of an intermediate host of different species. Most trypanosomes, for instance, utilize insects as intermediate hosts, but some species, *e.g.*, *T. evansi*, are transmitted directly by insects without any developmental cycle, and still others, *e.g.*, *T. equiperdum*, are transmitted directly from vertebrate to vertebrate by sexual intercourse. It is interesting to note also that, according to observations made by Gonder on trypanosomes (quoted by Nuttall), characters such as immunity to certain drugs, acquired by protozoans and maintained through thousands of asexual generations in vertebrate hosts, may be blotted out at a stroke in the invertebrate host cycle, which in itself suggests that some form of sexual reproduction, or at least a complete reorganization of the body, comparable, perhaps, to endomixis, occurs in the intermediate host. The great significance of this is evident: one of the difficulties connected with drug treatment of some protozoan diseases is the power of the protozoans to become immune to the drug when given in doses which are not destructive to the host; if such immunity is lost during transmission by an intermediate host there is no danger of an immune race of the parasite becoming permanently established. In like manner there is less danger of the permanence of strains which have become especially virulent for particular species of animals. Duke has adduced evidence that "cyclically" transmitted *Trypanosoma gambiense* do not develop as high a virulence for man as do trypanosomes transmitted directly by interrupted feeds.

Classification. — It is little wonder that such a varied assemblage of single-celled animals as constitutes the group Protozoa should be difficult to classify. It is obvious that these simple animals may be profoundly modified by their environment and such modifications can actually be seen in the course of the life history of many. The changes in form undergone by a trypanosome, for instance, under different environmental conditions and at different periods in the life history are represented in Fig. 34.

For a long time it was customary to divide the protozoa into four classes, — the Rhizopoda or ameba-like forms, the Mastigophora or flagellates, the Ciliata or ciliates, and the Sporozoa, or spore-forming parasitic forms. Doflein, however, modified this by first splitting the entire phylum Protozoa into two subphyla, the Plasmodroma and the Ciliophora, and this arrangement has been quite generally accepted by modern protozoölogists. The classification, as now usually accepted, is shown in the following outline:

Subphylum Plasmodroma. — Movement by means of pseudopodia or flagella; sexual reproduction, where known, by fusion of entire gametes.

I. Class: Rhizopoda (Sarcodina). — Body without a cuticle, but in many free-living forms protected by shells; movement ameboid by means of pseudopodia, at least as adults.

II. Class: Mastigophora. — Body usually with a definite cuticle; movement by means of one or more flagella; commonly known as flagellates.

III. Class: Cnidosporidia. — Parasitic ameboid animals which produce spores by a special method peculiar to themselves; spores provided with polar capsules from which long filaments can be extruded.

IV. Class: Sporozoa. — Parasitic forms which reproduce asexually by schizogony, and after sexual reproduction by formation of spores (or sporozoites) in cysts.

Subphylum Ciliophora (Infusoria). — Movement by means of cilia, which are present at least in some stage of development.

Group 1. Protociliata. — Two or more nuclei present, all of one type.

I. Class: Opalinata. — With the characters of the Group.

Group 2. Euciliata. — Two kinds of nuclei, macronucleus and micronucleus, present; sexual reproduction by conjugation, accompanied by disintegration of the macronucleus.

I. Class: Ciliata. — Cilia present throughout life.

II. Class: Suctoria. — Cilia present only in young stages, which usually attach themselves to objects, lose their cilia, and develop suctorial tentacles.

The class Rhizopoda (or Sarcodina) include mainly free-living forms inhabiting the ocean, fresh water and soil. Many of the marine forms are furnished with calcareous shells which are largely instrumental in building up chalk deposits. Only a few are parasitic, and these are all typical amebæ, which produce pseudopodia from any part of the naked body. The only form pathogenic to man is *Endamœba histolytica.*

The class Mastigophora includes a vast assemblage of organisms commonly called flagellates, many of which bridge the gap between plants and animals. Here again the majority of the included forms are free-living; many of them possess chlorophyll and live like typical plants, in fact are usually claimed by the botanists as well as the zoölogists. Many others, however, have cytostomes through which they ingest solid food like animals, and still others, like bacteria, absorb dissolved organic substances by osmosis through their cell walls. Such an organism as Euglena may be at once a plant and an animal. The parasitic species are all of animal nature, feeding either by ingestion, as in the case of many of the intestinal flagellates, or by osmosis, as in the case of the hæmoflagellates. Formerly the spirochætes were associated with the flagellates on account of a supposed relationship with the trypanosomes, but this idea has long since been exploded, and spirochætes are now placed in a group by themselves, associated with bacteria rather than protozoa, though in some respects they show affinity to the latter.

The class Cnidosporidia was formerly included with the Sporozoa, but these animals differ so widely in their life cycles that their separation is now quite generally agreed to Whether any form of sexual reproduction occurs is uncertain. The characteristic spores with polar capsules are formed in a different way than in any other protozoa; a single cell divides to form several cells, some of which give rise to polar capsules and others to spore membranes, while one or two alone survive to continue reproduction after germination. The Cnidosporidia are parasitic in cold-blooded vertebrates, insects, and other invertebrates; one of the best known is *Nosema bombycis*, the cause of pébrine in silkworms. Recently an organism named *Encephalitozoön* has been described as the cause of a disease of the central nervous system and kidneys of rabbits, and has been regarded by some workers as belonging to the Cnidosporidia, but it is by no means certain even that the organism is a protozoan. Levaditi, Nicolau and Schoen (1924) have suggested a similar affinity for the virus of rabies, which they think enters the body in an invisible stage and develops into the Negri body as a cyst stage, but there is no sound evidence for this view.

The class Sporozoa includes only parasitic forms, characterized by their multiplication by schizogony in the asexual phase, and by a similar formation of sporozoites in a cyst in the sexual phase; these two portions of the life cycle may, as in the malaria parasites, take place in alternate hosts. Many kinds of Sporozoa attack animals other than man, but man is parasitized by only a few. Among the few, however, are included the malaria parasites, which rank among the first of pathogenic organisms as regards significance to the human race as a whole. There are also a few coccidia which inhabit human intestinal cells, but man is exempt from attack by the majority of the Sporozoan groups, such as the Piroplasmidea, hæmogregarines, and true gregarines, which are so commonly found in lower animals, some of them causing important dieases even among mammals.

In addition to the known Sporozoa, there are a number of organisms, or supposed organisms, which are of problematical nature, by some workers believed to be related to the Sporozoa, and which may or may not be associated with diseased conditions. There are many such structures found in animals, such as the forms known as *Anaplasma*, *Toxoplasma*, *Grahamella*, etc., and some, such as *Rickettsia* and *Bartonella*, which cause important human diseases. The only reason for associating them with the Sporozoa seems to be want of a better place to put them. By some they are regarded as bacterial in nature, and others doubt whether they are living organisms at all. These forms will be considered in a separate section on " Obscure and Invisible Parasites," along with some of the so-called " filterable viruses."

The class Opalinata include ciliates which occupy an intermediate position between the more highly organized ciliates with functionally distinct nuclei and sexual reproduction by conjugation, on the one hand, and the Plasmodroma on the other. These forms, which have from two to very numerous nuclei, and sexually reproduce by fusion of entire gametes, as do the Plasmodroma, are nearly all parasites of the large intestine of amphibians, and do not concern us here.

The class Suctoria, which lose their cilia and acquire suctorial tentacles as adults, are for the most part free-living organisms attached to various objects in water, but a few are parasitic on ciliates, and one, *Allantosoma intestinalis*, is of interest as a parasite of ciliates in the cecum of horses.

The class Ciliata includes the most highly organized protozoa. The majority are free-living forms found in enormous abundance in foul water, hay infusions, etc., whence the old name, Infusoria. Many of them are inhabitants of the digestive canals of herbivorous animals, but since they prey on bacteria and débris in the intestine and do not attack the host itself, they may be regarded as commensals rather than parasites. A few forms are true pathogenic parasites, *e.g.*, *Balantidium*, which parasitizes man, pigs, and other animals.

Parasitism and Host Specificity.—There is no fundamental difference between free-living and parasitic protozoa in either structure, life-cycle or activities. It is very likely that parasitism among the protozoa arose in the first place by the ingestion of free-living forms by animals; some of these may be conceived of as having found conditions of life satisfactory in the digestive tracts of animals which devoured them; in the course of time such forms would become more and more perfectly adapted to the new environment, and eventually lose their power to live and reproduce in the outside world. Such parasitism would be expected to occur first in cold-blooded aquatic animals and subsequently to extend to warm-blooded land animals. It is significant that most of the common genera of intestinal protozoa of man, *e.g.*, *Endamœba*, *Chilomastix*, *Trichomonas* and *Giardia*, have representatives in the Amphibia, in some cases so closely similar to the human species as to have cast doubt on their specific distinctness. Many of the blood protozoa have undoubtedly arisen by a process only slightly more complicated. They first adapted themselves to the digestive tracts of invertebrates; in the case of blood-suckers they would then become adapted to living in the presence of the blood on which the invertebrates fed; having survived this probationary treatment, such parasites might then be capable, if inoculated into the blood stream or tissues of the vertebrates on which their invertebrate hosts habitually fed, of adapting themselves to life in this new environment, which had thus been approached in an indirect manner. There is little room for doubt but that the leishmanias and trypanosomes of vertebrates arose in this manner.

Even more than in the case of other parasites, the specificity of protozoan parasites for particular hosts is a much disputed question. The striking similarity between such parasites as the *Endamœbæ*, *Trichomonas*, *Chilomastix*, etc., in different species of mammals, together with the fact that nearly all of the species from man are transferable to rats and other animals, throws grave doubt on the idea of fairly strict specificity which has been advanced by some protozoölogists. There is, of course, no doubt but that all the species of *Trichomonas*, for example, have come from a common ancestor. Some, no doubt, have progressed to the point where they may be considered as well-defined species. Many others, however, seem not to have evolved so far, and to be still in the state of hostal varieties, *i.e.*, mere races of a single species, for the time being especially adapted to a particular host species by virtue of having lived in that host for some time. The question is of some importance from an epidemiological standpoint, since it involves the question of the extent to which lower animals may act as reservoirs for human parasites.

Importance. — Taken as a whole the protozoa must be looked upon as a group of organisms of prime importance as human parasites. Although Leeuwenhoek discovered the existence of protozoa over 250 years ago, the first parasitic species, *Balantidium coli*, was not discovered until 1856. At the present time a large proportion of medical practice and disease prevention in tropical countries, and a considerable proportion in all countries, depends on our knowledge of the habits and life history of parasitic protozoa, nearly all of which has been gained in the last 50 years, and much of it since the beginning of the present century. Almost daily new discoveries in connection with disease-causing protozoa are being made; there are few branches of scientific research which offer a brighter or more promising field of endeavor for students at the present time than the investigation of pathogenic protozoa.

The diseases caused by protozoa are fundamentally different in nature from those caused by the majority of bacteria. When most kinds of bacteria invade the body and cause infection, a sharp battle ensues between the invaders and the defenses of the host, and it is a battle which continues unabated until either the host succumbs and dies, or the bacteria are completely destroyed, with not a survivor left. The only outstanding exception to this is in the case of the so-called acid-fast bacteria, causing tuberculosis and leprosy, in which, after a preliminary struggle, a sort of truce is struck and the disease tends to settle down to a comparatively mild, chronic state in which there is a sort of balance of power between invader and host, each one, however, ready to take advantage of the slightest circumstance which tips the balance one way or the other. Structurally the acid-fast bacteria differ from other bacteria in possessing a very resistant waxy envelope which renders them immune to the attacks of the leucocytes which devour and digest other kinds of bacteria, and it is undoubtedly to this that these organisms owe their ability to live on in a state of suppression in a host which has gotten them under control. Now protozoa without exception resemble the acid-fast bacteria in this respect. They cause diseases which often, after an initial flare-up, become chronic in nature, and may persist for years, sometimes even for life. Often there are no symptoms whatever, but the parasites, suppressed but not destroyed, are ready to stage an insurrection the moment the resistance of the host is weakened by other invasions, or by exhaustion, malnutrition, etc. The protozoa, like the acid-fast bacteria, undoubtedly owe their survival to their relative immunity to the attacks of leucocytes, but this immunity is not due in this case to a non-digestible capsule, but to their animal nature. Leucocytes are cells of the body which, through countless ages of specialization of other cells, have retained their primitive nature and habits, and are themselves not essentially different in these respects from the protozoa themselves. Whereas leucocytes swoop down upon invading vegetable cells or other unrelated substances in devastating swarms, they seem to fail to recognize protozoa as enemies, or rather as prey; the protozoa, as it were, escape the military police of the host by passing unrecognized as foreigners. Some of them appear to be ingested by leucocytes, *e.g.*, *Leishmania donovani*, but perhaps in these cases the parasites and not the leucocytes are the aggressors; in other words, the leucocyte may not have ingested the protozoa, but the protozoa may have invaded the leucocytes. An excellent example of the difference between the reaction of leucocytes to bacteria and to protozoa can be seen in a comparison of bacillary and amebic dysentery. In the former the invaded tissues are crowded with actively feeding leucocytes, and the stools are full of these pus cells; in amebic dysentery, although the lesions are deeper, there is no pus at all, and no leucocytes in evidence. When the blood stream is invaded by streptococci, there is a striking increase in leucocytes in the blood (leucocytosis); but when the blood stream is full of malaria parasites or trypanosomes, no such effect is in evidence. In the case of organisms which do not actually invade the tissues, such as colon bacilli in the urinary bladder, typhoid organisms in the gall bladder, etc., chronic bacterial infections may occur, and this would naturally be expected of protozoa also, which is actually the case. It is in the blood- and tissue-invading forms that the difference is so striking. The dysentery amebæ, trypanosomes, leishmanias, malaria parasites, coccidians, *Balantidium*, etc., — all tend to cause chronic and long-enduring infections. In bacterial infections drug treatment is seldom if ever of any avail; instead recovery is assured or hastened by stimulating the natural defenses of the host by means of vaccinations or serum treatment. In protozoan infections, on the other hand, such methods have never succeeded, and treatment with specific drugs is necessary, *e.g.*, emetin for amebæ, antimony for leishmanias, quinine for malarial parasites, etc.

It is interesting, and perhaps suggestive, that in these respects the spirochætes are definitely aligned with the protozoa, and the rickettsias and insect-borne filterable viruses (yellow fever, dengue and papatasi fever) with the bacteria.

CHAPTER IV

SPIROCHÆTES

General Account. — On the vague unsettled borderline between bacteria and protozoa there is a group of organisms which are waging a frightful war against human life and health. These organisms, commonly known as spirochætes, when first discovered were supposed to be of bacterial nature. Later, largely as the result of a now historically famous error made by Schaudinn, in which he mixed up and confused the stages of development of several different parasites in the blood of an owl, the spirochætes came to be regarded as protozoa, closely related to the trypanosomes. Strangely enough, although nearly all treatises on bacteria as well as protozoa give some account of the spirochætes, they are still dealt with much more extensively in protozoölogy than in bacteriology books, although the authors disclaim any notion that they are really protozoa. They are too important to be neglected, and until the bacteriologists are willing to assume full responsibility for them, the protozoölogists will have to care for this orphan which Schaudinn left on their doorstep.

Like bacteria the spirochætes lack any distinct nucleus; their multiplication is by transverse division and not longitudinal as in flagellates, with which group they would have to be associated if placed in the protozoa at all; they are not oriented into an anterior and posterior end; the flexible limiting membrane of the body is not like that of the protozoa; and there are now believed to be no flagella or other organs of locomotion. For a time the method of transmission of spirochætes by intermediate hosts, and the assumption of a definite cycle of development in these hosts, was used as an argument in favor of their protozoan affinities; but it is not certain that such a developmental cycle occurs, or that the transmission by ticks and lice is essentially different from the transmission of plague by fleas. Even if a developmental cycle is proved, it would not make it necessary to assume protozoan affinities, for many single-celled alga-like forms have complicated life cycles, and there is as much reason for associating the spirochætes with the algæ as with the protozoa.

There are several different types of spirochætes. The true genus *Spirochæta* (Fig. 5*A*) include very long (200–500 μ) and relatively large organisms which have a central axis or filament around which the body is wound, like a piece of rubber tubing wound around a wire, as Wenyon expresses it. The body protoplasm has vacuoles in it, and a series of deep-staining granules which may or may not be chromatin. The genus *Cristispira* (Fig. 5*B*) includes large forms (45 to 100 μ long) found in the crystalline style of molluscs. The body is cylindrical and divided internally into short segments, somewhat like a bamboo stem; it is thrown into coarse spirals and has a flexible spiral membrane, the crista, appearing like a raised ridge along the concavity of the spirals. The other spirochætes are so small and exceedingly slender that very little can be found out about their structure. The only certain knowledge about them is that they have very flexible bodies, spirally twisted like corkscrews; some observers have described a crista, others one or more polar flagella, and others a series of internal granules which become the centers of spore-like bodies into which the organisms are supposed to break up. None of these observations can be accepted as definitely proved. According to Zuelzer the small spirochætes have essentially the same structure as the large *Spirochæta* and can therefore be included in the same genus, but this view is not yet widely accepted. These spirochætes are very active in movement, and dart back and forth across the field of a microscope so swiftly that they can hardly be followed by the eye. The movement is apparently by wave motions passing through the body, accompanied by a rotation of the body in corkscrew fashion. Swiftly moving spirochætes show many small waves in their bodies, while the more slowly-moving ones have larger and more graceful curls. They also have the power of bending their bodies to and fro, and of oscillating while attached to some object by one end. Spirochætes divide by a transverse division of the body into two, preceded by a fine drawing out of the delicate cell membrane between the two parts, like a glass tube drawn out after heating. Probably the fine filaments sometimes seen at one or both ends of a spirochæte are the remains of this drawn-out membrane, and not flagella as sometimes thought. Often two incompletely separated spirochætes twist about each other, giving the appearance of having split longitudinally. In healthy living spirochætes, when relaxed, the axis of the body is a straight line, but after being dried, as in blood films, they may become distorted, and the actual spirals be

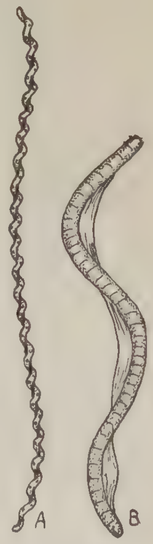

FIG. 5. *A*, *Spirochæta plicatilis*, *B*, *Cristispira balbianii*; diagrammatic. × 2000. (Partly after Zuelzer and Wenyon.)

obliterated. Figure 7 shows the appearance of relapsing fever spirochætes when living and after being dried and stained. A number of observers have described a breaking up of spirochætes into minute granules, and a subsequent growth of spirochætes from such granules (see p. 53), but the occurrence of such a phenomenon, while not impossible or even unlikely, has not been sufficiently confirmed.

The spirochætes, other than true *Spirochæta* and *Cristispira*, are now usually placed in two genera, *Treponema* and *Leptospira*. The genus *Treponema* until recently was reserved for spirochætes with short kinky coils, such as *T. pallidum* of syphilis, while the blood spirochætes, such as *T. recurrentis* of relapsing fever, which have larger, more graceful coils, were separated into a genus *Spironema* or *Spiroschaudinnia*, but these two types differ only in size and number of coils, and there are all gradations between them, hence they are here all grouped together. The genus *Leptospira* consists of excessively delicate forms in which the spiral rope-like windings are so minute as to be invisible in ordinary stained preparations, but visible under a dark-field microscope, and which show a few gross undulations of the body, which is usually hooked at the ends. Both of these types of spirochætes must be distinguished from the bacterial genus *Spirillum*, which contains organisms with rigid preformed spirals, and with terminal flagella. The organism causing rat-bite fever, described by Japanese workers as *Spirochæta morsus-muris*, has been shown to be really a *Spirillum*, *S. minus*. Species of both *Treponema* and *Leptospira* occur in fresh water as well as in the bodies of animals as saprophytes or parasites. Some of these free-living forms, when cultured and inoculated into animals, are pathogenic.

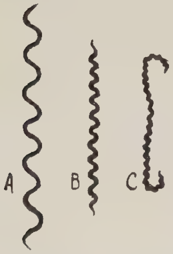

FIG. 6. Types of spirochætes. *A*, *Treponema recurrentis; B*, *Treponema pallidum; C*, *Leptospira icterohæmorrhagiæ*. × 2000.

The various species of *Treponema* differ from each other in the length and coarseness of the body, in the number of spirals in a given length, and in the rounded or tapering form of the ends of the body. Many of the species described are indistinguishable morphologically, and are only recognizable by their pathogenic effects, places where found, immunological reactions, and methods of transmission. The relapsing fever spirochætes, for instance, have been regarded by many workers as constituting many different species, separable on the basis of transmission by ticks or lice, and cross-immunity tests between types. Likewise many different species have been described from normal and diseased conditions in the mouth, tonsils, lungs, intestine, skin ulcers, etc., which are not distinguishable morphologically. Wenyon thinks it is not an unreasonable hypothesis to suppose that there are one or more saprophytic spirochætes which can invade any part of the body, provided a suitable environment exists. At present it is impossible to classify the species of *Treponema* other than by their pathogenicity or otherwise, the types of infection produced, and the situations where they occur. The spirochætes of syphilis and yaws, for instance, cannot be distinguished with certainty from a form which occurs almost universally in normal mouths, on the tartar and about the roots of the teeth, and which is apparently perfectly harmless.

Spirochætes and Disease. — There are several human diseases for which spirochætes are unquestionably responsible, among which are relapsing fever, syphilis, yaws, and infectious jaundice, and there are many other diseased conditions with which spirochætes are associated, and for which they are in part, or at times, responsible. The mere presence of spirochætes in sores or diseased tissue, however, is not sufficient reason for believing that they are the direct cause of the diseased condition, for, like many bacteria, they are often found in exposed sores which are known to be due to other causes. Spirochætes are often found associated in sores or ulcers with various kinds of bacteria; in Vincent's angina a spirochæte and a fusiform bacillus appear to be jointly guilty, the two living together in a sort of symbiotic relationship.

In general the diseases caused by spirochætes may be divided into four main groups. First, there is the type in which the spirochætes live and multiply mainly in the blood. The various forms of relapsing fever belong to this group. Formerly rat-bite fever was also included here, but the organism which causes it is now regarded as a *Spirillum* rather than a spirochæte. Second, there is the type in which the spirochætes make a general invasion of the body and live primarily in the tissues, often localizing in particular tissues or organs after the preliminary general invasion. To this type belong syphilis and yaws. Third, there are local infections or lesions in which spirochætes may be present in large number, and may or may not be the sole or primary cause. To this belong Vincent's angina, spirochætal bronchitis, tropical ulcers, ulcerating granuloma, etc. Fourth, there are the *Leptospira* diseases, in which spirochætes of the genus *Leptospira* invade the body and localize primarily in the liver and kidneys. To this belong infectious jaundice and Japanese seven-day fever; much evidence was adduced by Noguchi to show that yellow fever is also a leptospiral disease, and other investigators have reported finding leptospiras in dengue and sandfly fever cases, but all of these diseases are really caused by filterable viruses.

Relapsing Fever

In every continent in the world, with the possible exception of Australia, there occurs a form of relapsing fever caused by spirochætes in the blood. In Africa it ranks next to malaria and sleeping sickness as a scourge of that disease-cursed country. In India it is hardly less severe, while in Eastern Europe and America it is a mild disease. The clinical effects of the various strains of the disease vary, especially in the number and duration of the relapses.

Although relapsing fever was known to physicians over a century ago, it was not until 1873 that Obermeier discovered the hitherto unseen agitator which causes it; he made his discovery during one of the epidemics which spread from Russia over Poland and Prussia.

Many great epidemics have swept Russian, Austrian and Balkan cities. Early in the great European war Serbia was held in the grip of an epidemic of relapsing fever of unusual severity and high fatality. In Bombay and other Indian cities the oriental type of the disease is nearly always present, and it sporadically appears in various parts of North Africa, China and Japan. In tropical Africa it occurs over a large part of the continent occupied by the tick which transmits it. It is also probably widely distributed throughout Mexico and Central and South America. In the United States it occurs chiefly as irregular epidemics among immigrants.

After successful recovery from an attack of one strain, an immunity to that particular strain is developed, but this does not protect against other strains. There is also a difference in the susceptibility of experimental animals to the different strains, and the method of transmission varies in different parts of the world, but experiments have shown that with respect to at least some of the strains their transmitters, lice or ticks, are interchangeable. On account of these variations, together with supposed average differences in size and number of coils of the parasites, the spirochætes of the various forms of relapsing fever have been given different species names; the points on which the differentiations are made, however, (mainly immunological tests and method of transmission) are not valid characteristics on which to separate species, therefore most protozoölogists at present recognize only one species, *Treponema* (or *Spirochæta*) *recurrentis*, and designate the various strains as varieties or races. Morphologically similar spirochætes, *T. anserinum*, cause a serious disease of fowls, geese, ducks and other birds. Other similar spirochætes, named *T. theileri*, occur in the blood of cattle, sheep, horses, etc., but do not cause symptoms, and spirochætes closely resembling the human species occur in monkeys. In Dakar a blood spirochæte, named *T. crociduræ*, occurs commonly in shrews, and this form has been shown to be immunologically identical with the human relapsing fever spirochæte of the same region. Similar if not identical spirochætes occur in various other small mammals in Africa, such as the desert gerbille (*Meriones shawi*) of North Africa, the "gondi" of Tunis, and the field vole of Dakar. The latter has been shown to be transmissible to man. Nicolle and Anderson think it is very likely that the relapsing fever spirochætes were originally parasitic in small African rodents, and were transmitted among them by ticks. The ticks transmitted them to man, and finally, as the result of close association with lice feeding on infected human beings, the parasites adapted themselves to survival in the bodies of these insects, which then assumed the rôle of transmitters.

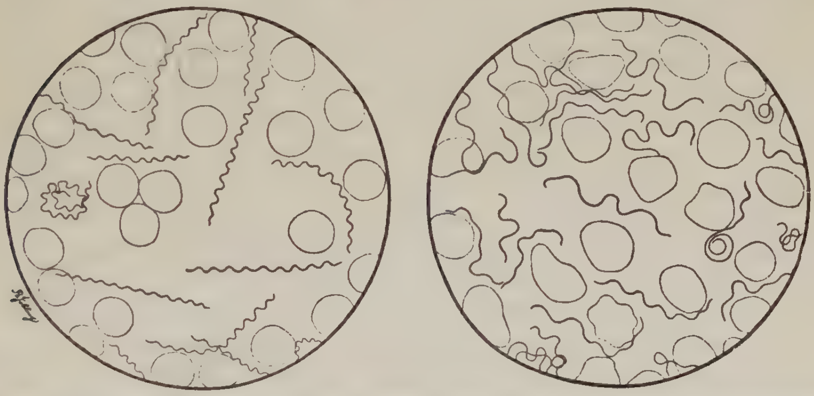

FIG. 7. *Treponema recurrentis*, var. *duttoni*, showing appearance of spirochætes when living (left), and on a dried and stained slide (right). × 1000. (After Wenyon, "Protozoölogy.")

Treponema recurrentis is a very active organism; when alive it nearly always holds its body in a straight line, except to make its way between blood corpuscles, and proceeds in either direction by rapid spiral undulations of the body. It is usually from 10 to 20 μ in length, averaging about 15 μ, and has a series of regular, graceful spiral turns of the body, each occupying from 2 to 3 μ of the length. The ends of the body taper slightly. The spirochætes may be extremely numerous in the blood, especially during the active phases of the disease, but they become very scanty, and often impossible to find, during the intermissions between relapses. When blood films are dried the spirochætes become distorted and show irregular coarse spirals of quite a different nature from those present in the living organism (Fig. 7). When an infection is being recovered from and antibodies are present in the blood, the spirochætes show degenerative changes, and are seen clumped together and variously coiled.

Another peculiar phenomenon exhibited by them in blood which has become immunized, as is also the case with trypanosomes, is that known as the Rieckenberg phenomenon; the organisms acquire the property of causing blood platelets to adhere to them until they become laden with them. This reaction is strictly specific and can be used in identifying strains of spirochætes or trypanosomes. Another very interesting phenomenon is the immunological distinctness of the strains of the spirochætes which occur in the original infections and in relapses, first worked out in detail by Cunningham (1925) and added to by Meleney (1928); this peculiarity, too, is shared by trypanosomes. In the case of Cunningham's Indian strain of the spirochætes usually only one relapse occurs, but if a second one develops, the spirochætes then present are similar to the original infection strain. Thus if we call the infection or passage strain " A " and the relapse strain " B ", in a series of relapses the strains present will be A, B, A, B, etc. Meleney, however, in China, obtained six different strains; their sequence in relapses was not always the same, for in some relapses new strains were produced while in others there was a reversion to an earlier strain. This situation is strikingly similar to that existing among trypanosomes in relapses (see p. 20). In view of these interesting developments and the demonstration of different immunological strains in single areas and epidemics, and even in individual cases, doubt arises as to the validity of the immunological differences between geographic strains of relapsing fever spirochætes unless all the possible relapse strains of one were compared with those of the other.

Transmission. — Relapsing fevers are commonly divided into two groups, (*a*) those transmitted by ticks of the genus *Ornithodoros* (see p. 427) and characterized by a number of short attacks at short intervals, and easily transferable to white rats and mice, and (*b*) those transmitted by lice, and characterized by a smaller number of longer attacks occurring at longer intervals, and not easily transferred to rats and mice. Tick-borne strains occur in Central Africa, Persia and Central Asia, Spain and Morocco, and in Central and South America, while louse-borne strains occur in North Africa, West Africa, Europe, India, China, and United States. The West African louse-borne strain seems to have been introduced since the great war, probably from Europe. The sharp line of distinction between these two groups is, however, breaking down, for evidence is accumulating that ticks of the genus *Ornithodoros* are capable of transmitting all strains, and do so wherever species which habitually bite man occur in abundance. There is much to favor the view of Nicolle and Anderson, that human relapsing fever is a by-product of a rodent disease transmitted by ticks, such as the spirochæte infection of North African gerbilles transmitted by *Ornithodoros normandi*; that after establishment of the disease in man by ticks, the spirochætes adapt themselves to development in lice; and that in countries where lice are prevalent epidemic relapsing fever may occur in the complete absence of *Ornithodoros*. Such a change-over from endemic tick-borne relapsing fever to the epidemic louse-borne disease seems to be of frequent occurrence in Tunis. The disease is kept alive in the south by tick transmission, and from this stronghold louse-borne epidemics periodically sweep north.

In Central Africa the disease is known as "tick fever," and was thought to be the result of the poisonous nature of the bite of the common house-infesting tick, *Ornithodoros moubata* (see p. 427 and Fig. 199), until Ross and Milne (1904) and independently Dutton and Todd (1905) showed that this disease was caused by spirochætes transmitted by the tick. It was evident, however, that some other form of transmission occurred in other countries where *Ornithodoros* was absent or rare. In 1907 Mackie collected epidemiological evidence against lice as transmitters, and found spirochætes in abundance in these insects fed on cases of the disease; other investigators got similar evidence in Algeria and Egypt. The mechanism of transmission and final proof of the rôle of lice was worked out by Nicolle, Blaizot and Conseil in 1912.

The course of events in ticks and lice is not exactly the same. Ticks are continuously infective from within an hour after infection up to at least a year and a half afterwards, and the infection is transmitted through the eggs to the second and even the third generation of ticks. According to some investigators the spirochætes break up into minute granules in the Malpighian tubules, and this is regarded as a method of multiplication which occurs at low temperatures. These granules appear to penetrate many of the organs of the tick, including the ovaries and eggs. When ticks containing such granules are exposed to a temperature of 95° F. for a few days, orthodox spirochætes reappear. Leishman (1920) believed that he could observe the growth of spirochætes from the granules. Balfour, Fantham, and others have observed a similar phenomenon in the fowl tick, *Argas persicus*, infected with *T. anserinum*. The interpretation of the life cycle on this basis is shown in Fig. 8. Others, however, believe that the granules may represent degenerating spirochætes, or may be entirely unrelated to spirochætes, since Wittrock (1913) claims to have observed them in uninfected ticks; they may possibly be of the nature of *Rickettsia*. It is a fact, however, that in a few days the spirochætes disappear from the digestive tract of the tick and later reappear in increasing numbers in the body cavity and tissues; but, as Wenyon points out, it is just as reasonable to assume that they are present, but are at first too few in number to be detected, as to suppose they occur in granule form. The granule phase of spirochætes must at present be accepted with mental reservations.

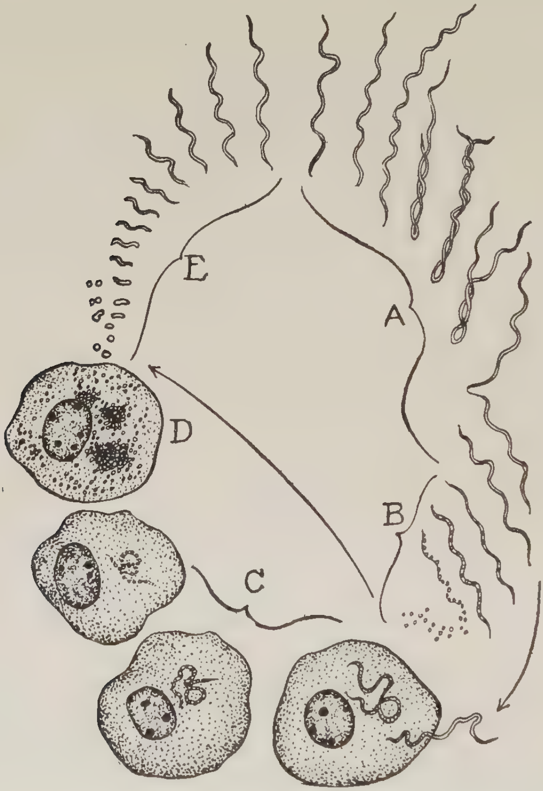

FIG. 8. Life cycle, according to Hindle, of *Treponema anserinum*, applicable also to *T. duttoni* of relapsing fever. *A*, multiplication by transverse division in vertebrate blood; *B*, formation of coccoid bodies in vertebrate blood; *C*, infection of cells of tick and formation of coccoid bodies; *D*, multiplication of coccoid bodies in tick; *E*, development of spirochæte forms from coccoid bodies after reëntering vertebrate blood. × 1500. (After Hindle.)

Whether the spirochætes multiply as such or by formation of granules, they extensively invade the body of the tick, and are present in most of the organs and tissues of the body as well as in the celomic fluid. The coxal fluid exuded by ticks when feeding is infective, and it is also claimed that the feces are infective, although spirochætes have not been found in them. The salivary glands also become infected, so it is probable that infection can come from direct injection as well as from contamination of the bites.

The transmission of the organisms to the young through the eggs results in the offspring of infected ticks being as dangerous as their parents. Indeed the tiny unfed nymphs are particularly dangerous, since they escape detection by their small size.

The cycle of development in lice is similar in most respects, but in this case the lice are definitely not infective for some days after feeding on a relapsing fever case. According to Nicolle and his colleagues, the spirochætes at first apply themselves to the walls of the stomach and penetrate into the cells, but within 24 hours they entirely disappear without leaving a trace. For from 6 to 8 days the spirochætes can be found nowhere in the lice, and during this period the lice are not infective, but at the end of this time the spirochætes begin to reappear, this time in the fluids of the body cavity; they gradually increase in numbers, and penetrate with the body fluid even to the tips of the legs and antennæ. They remain present in the lice up to the 19th to 25th day after the infective feed, and during this time the louse is capable of transmission of the disease. It is not by the bites of the lice, but by crushing of the body or breaking off of an appendage and allowing the juices from its body cavity to contaminate the wound that infection is brought about. In one case a man experimented upon in Algeria was bitten 30,000 to 40,000 times by infected lice without contracting the disease, when the lice were gently handled to prevent injuring them; but one louse crushed, and the body fluids placed on the conjunctiva or rubbed into a bite on the skin, causes the disease to develop.

In a few cases infection passes through the eggs of lice to the next generation, as in the case of ticks, but this is exceptional.

There is no good evidence that the disease is normally transmitted in any other way than by *Ornithodoros* (and possibly *Argas*) and lice. Bedbugs have frequently been suspected (see p. 448), but although these insects harbor the spirochætes in their body cavities for a long time, and are infective if their macerated bodies are injected into animals, it is practically certain that bugs cannot transmit the disease by their bites; occasional cases might be caused by the crushing of infected bugs, but all the available evidence is against bugs playing any important rôle in connection with relapsing fever.

The Disease. — After an incubation period lasting from two days to two weeks, the initial attack begins suddenly. The temperature rises rapidly and lasts for from 4 to 6 days. Then comes a crisis; the temperature falls to normal or below, and the patient recovers so rapidly and completely that he thinks it unnecessary to remain in the hospital any longer. Then, 7 to 9 days after the first crisis, comes a relapse, with a repetition of all the symptoms. Following this there comes a second crisis and a period of apparently normal health, which may be permanent or may be followed by more relapses. In general the louse-borne types have only one or two relapses, while the tick-borne types are likely to have 4 or 5 or even more, of shorter duration and more irregular in occurrence. The mortality is usually low, but varies in different epidemics.

The first onset of fever is accompanied by appearance of spirochætes in the blood, much more abundantly in some cases than in others. At the crisis the organisms disappear very rapidly, no doubt being destroyed by some type of antibody from which a relatively few individuals escape, possibly due to their situation outside the blood stream, where they may have time to undergo the necessary physiological change which enables them to resist the destructive action of the blood. The multiplication of this relapse strain brings on the first relapse, and any subsequent relapses are brought on in a similar manner. The spirochætes are not confined to the blood, but undoubtedly penetrate extensively into the tissues, and in experimentally infected mice they regularly penetrate into the cerebro-spinal fluid and brain, and no doubt do so in man, too; their occurrence in human cerebro-spinal fluid has frequently been demonstrated. It has also been claimed that they occur in the urine, which would appear more probable than otherwise.

Treatment and Prevention. — Ehrlich's famous spirochæte poison, "No. 606," or salvarsan, and many other allied arsenical preparations which have subsequently been developed as improvements or substitutes for it, are very effective in the treatment of relapsing fever, especially if injected intravenously before the first crisis or in the febrile stages of relapses. Experiments on mice indicate that spirochætes located in the brain are not destroyed. Novy and Knapp have shown that inoculation of the serum of highly immunized animals protects experimental animals, and when injected into infected animals has a curative effect. So far, drug treatment has been preferred to serum treatment in the case of human infections.

Eradication of vermin from person and home and avoidance of places where infected parasites might be acquired are the most important protective measures in places where an epidemic is raging. Methods for the control of ticks are discussed on page 430, and of lice on page 475. Since the parasites are not ordinarily introduced directly into the blood by the beak of the transmitter, but are simply voided with the excrement in the vicinity of the wound, careful disinfection, with alcohol or carbolic acid, of the wound before the removal of the parasite is a good means of prevention if the suspected transmitter be caught in the act of biting.

Syphilis

History. — There are few diseases which mean more to the human race as a whole than syphilis, due in part to its almost universal distribution, and in part to its insidious and deceiving course, thereby leading to untold misery and disaster. Rosenau says " civilization and syphilization have been close companions "; the one has followed in the wake of the other like the guerillas behind an army. Unlike most diseases, syphilis is one of whose origin among civilized nations we have strong evidence. There are many reasons for believing that syphilis was acquired by the members of Columbus' crew when they discovered the island of Haiti, and that it was carried back to Spain by them on their return. These adventurers promptly joined the army of Charles VIII of France in its invasion of Italy in 1494. Soon after the army had triumphantly set up a court in Naples it became weakened through the ravages of a terrible venereal disease of unusual intensity, hitherto apparently unknown in Europe. The following year the army retreated almost in a rout and was broken up, the miscellaneous troops scattering all over Europe to their respective home countries, and carrying the new disease with them. In the next four years the disease had spread to practically every country in Europe, and was soon carried by the Portuguese to Africa and the Orient. The venereal nature of the disease was fully recognized, and its foreign origin was well known, each nation trying to shift the responsibility to another by name, many peoples calling it the " French disease," others the " Spanish disease," etc., while the Spanish alone seemed aware of its real origin in America and called it " española " which then meant Haiti. The absence of any reference to a disease resembling syphilis in the historical records before the discovery of America; the absence of any bones showing evidence of syphilitic attack in the abundant pre-Columbian remains in Europe, and abundance of such bones in American remains, many of which must certainly be pre-Columbian; the positive evidence of Spanish physicians and historians at the time of the return of Columbus; and the severity of the great epidemic in the latter part of the 15th century, — it being almost invariable for an infectious disease, when first introduced among a new people, to rage with unwonted severity; all these facts point strongly to the American origin of syphilis at least so far as Europe is concerned, but it is claimed that the Chinese were acquainted with the disease 2000 years B.C.

Interesting as is the early history of the disease, the recent history is infinitely more so. By the beginning of the 20th century medical men had come to the end of their rope in knowledge and treatment of the disease, and found themselves at a standstill. But in 1902 the disease was successfully transmitted to animals where it could be conveniently studied; in 1905 Schaudinn discovered the causative organism, *Treponema pallidum* (Fig. 9), which is believed to cause the disease. In 1906 Wassermann demonstrated the possibility of detecting latent syphilis by the reaction which bears his name; in 1910 Ehrlich made the epoch-making discovery of his famous drug, " No. 606," or salvarsan, a deadly poison for spirochætes of all kinds, and a cure for syphilis in nearly all stages; in 1913 the direct relation of syphilis to insanity, paralysis and other diseased conditions of the central nervous system was demonstrated by the discovery of the organisms in the cerebrospinal fluid, and in the same year a method of destroying the parasites in the central nervous system was discovered. There is no other instance in the history of medical science where such wonderful strides have been made in such a short time in the knowledge and control of a disease. At the beginning of the twentieth century syphilis was one of the most horrible, hopeless and tragic diseases known to ravage the human body; it is now a disease which can be readily recognized even in latent stages; it can be cured in its early stages; and the terrible tragedies resulting from apparent but imperfect cure can be avoided. Its eradication, however, will not soon, if ever, be accomplished, since in this are involved some of the most intricate moral and social questions with which we have to deal.

Prevalence. — The prevalence of syphilis is difficult to determine, for at present the recording of syphilitic cases is practiced to a very slight extent, and accurate data can be obtained only in military organizations and certain public and private institutions. Sir William Osler places syphilis as third or fourth of the killing diseases. The use of the Wassermann reaction fo the detection of syphilis has greatly extended the possibility of arriving at an estimate of the prevalence of the disease, and has shown that it is far more common than was formerly believed. Yet even the Wassermann test fails in about 10 per cent of cases. It is now known that the disease may be present in latent but nevertheless infective form for many years after all active symptoms have disappeared. The disease invades alike the palace of the millionaire and the hovel of the tramp, but all classes of society are not equally attacked. In general the prevalence of syphilis increases as we descend in the social scale. It is much more prevalent, in America, among negroes than among whites. A report of the British Royal Commission on Venereal

Diseases in 1916 concluded that the number of people infected with syphilis cannot fall below 10 per cent in large cities, and that at least one-half the registered still-births are due to this disease. They found that in Britain this as well as other venereal diseases is most prevalent in the unskilled labor class, and least among miners and agricultural laborers. Fournier estimated that in Paris 15 per cent were infected. In China syphilis is, next to tuberculosis, the most common disease. In the " red light " districts of cities, which undoubtedly serve as the centers of distribution for the disease, the per cent of syphilitic prostitutes is very high. Dr. Browning found every one of 104 prostitutes in Glasgow infected, and a like condition among 109 men, women and children classed as " vagrants."

In the United States, syphilis is commoner in the extreme southern States than in northern or western ones, partly on account of the higher percentage of negroes. Hazen (1928) summarizes the situation as follows: " A study based on cross sections of the population of the United States according to age, sex, race, residence, and economic condition shows that there are probably about eight million syphilitics in the country." Army statistics collected by Vedder indicate that among young men in civil life, between the ages of 20 and 30, the incidence of syphilis is about 20 per cent. " It means that when a man's daughter marries, the chances are just one to five that she will become the victim of ' damaged goods '." Even in the relatively select class of West Point cadets, from 2 to 5 per cent are probably syphilitic. The figures obtained from an examination of 531 Porto Rican enlisted men are most startling of all — over 50 per cent showed evidence of being probably syphilitic.

Transmission. — Syphilis, at least in temperate climates, is fundamentally a venereal disease, transmitted by sexual intercourse, and over 90 per cent of cases are undoubtedly of such origin. It is a common belief that this is the only way in which the disease can be acquired, and sometimes an unjust stigma of shame and disgrace is attached to a perfectly innocent case of syphilis. As already remarked, in the vast majority of cases the parasites are directly acquired from their usual habitat in the underworld, but the disease is very often transmitted after marriage to husband or wife, and from parents to children, either before birth, by nursing, or by indirect contact. A horrible case is on record where seven young women at a church social in Philadelphia acquired syphilis from kissing a young man who had a syphilitic sore on his lip. A case recently occurred in one of our western cities which was ultimately traced to the eating of apples sold by an Italian who was in the habit of spitting on his fruits and rubbing them on his sleeve to shine them. Public drinking cups, public towels and soiled bed-linen serve admirably as temporary abodes for the spirochætes of syphilis, but fortunately these curses of civilization are in most places abolished by law. Unsanitary barbers and dentists can easily spread infection, and dentists and physicians often themselves contract the disease from handling syphilitic patients, the spirochætes readily entering the smallest cut or abrasion of the skin. Midwives and wet nurses are likewise exposed to infection from diseased babies, as are the babies from diseased nurses. Indeed, when we think of the many ways in which syphilis spirochætes may be transmitted from person to person it is surprising that the number of innocent cases is not much greater.

In the tropics the disease is less consistently venereal, and is commonly acquired in childhood, with resultant immunity later in life. Hudson (1928), for example, describes this type of syphilis as practically universal among the Syrian Arabs, by whom it is called " bejel "; it is not considered a venereal disease. Where such a disease occurs along with yaws (see p. 69), it is not surprising that the two are confused, whether rightly or wrongly.

The Spirochætes. — The spirochætes of syphilis, *Treponema pallidum* (Fig. 6*B*), vary in length from 4 to 14 μ and are immeasurably slender. They are more closely curled than the spirochætes of relapsing fever, having usually from 6 to 14 very regular, short, sharp curls. Each coil occupies about one micron. The living organisms are very active and dart with great speed across a slide, threading their way between blood corpuscles or cells. The spiral turning of the body reminds one of the undulating movements of a swimming snake. Another spirochæte, *T. refringens* (Fig. 9), is often found associated with *T. pallidum.*

This spirochæte is larger, with loose open coils, and when observed under a dark-field microscope is brilliant white and refringent, whereas *T. pallidum* has a pale-white, dull, silvery appearance. When viewed slightly out of focus, *T. refringens* and most other spirochætes take on a rusty appearance, whereas *T. pallidum* looks dead-white. Other spirochætes which may be found when *T. pallidum* is looked for are mostly coarser and have larger coils. A common mouth spirochæte, *T. microdentium*, is strikingly similar, but gives a rusty instead of dead-white tinge when the objective is raised slightly above focus.

During the early stages of their sojourn in the body the spirochætes can always be found in the primary and secondary lesions, and in the neighboring lymph glands. During the second phase of the disease and also toward the end of the first phase the spirochætes occur in variable numbers in the blood, and very early make their way into the cerebrospinal fluid in the brain and spinal cord. After it was found that the spirochætes actually invade the central nervous system, and cause diseases of it, it was supposed that this occurred only occasionally in late stages of the disease. Later it was shown, however, that the great majority (80 per cent) of syphilitics show distinct pathological changes in the spinal fluid, due to spirochætes in it, from the date of the primary sore, and are therefore possible candidates for syphilis of the nervous system. During the second phase the spirochætes make a general invasion of the entire body, later showing some special predilection for certain tissues or organs. The gummy sores or "gummas" which often break out during the third stage of the disease have usually been considered non-infective, and spirochætes could not be found in them. Recently, however, the parasites have been found in some of these lesions, also. In congenital syphilis the parasites often multiply in enormous numbers in the unborn child, penetrating practically every organ and tissue of the body. The liver especially is often found literally teeming with spirochætes (Fig. 10).

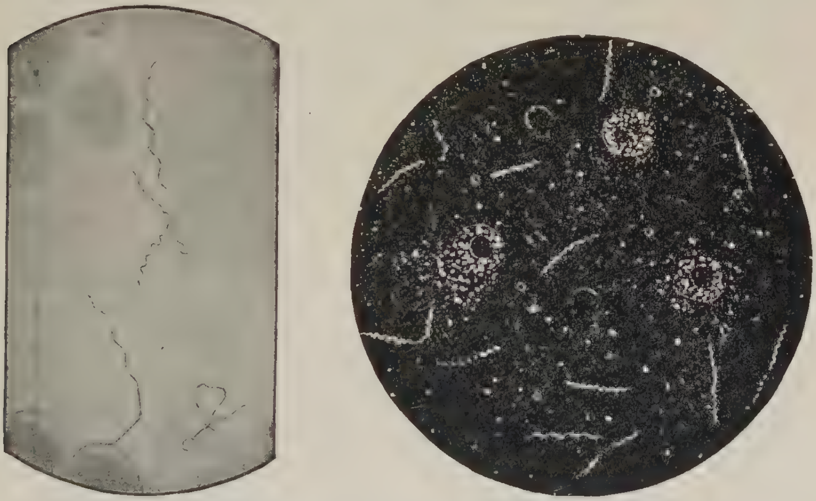

Fig. 9. Left, spirochætes from a syphilitic lesion; the two in the center are *T. pallidum*, the others *T. refringens*. From Schaudinn and Hoffman. Right, *T. pallidum* appearing as bright refractile objects under dark-field illumination. (After Park and Williams, from Gershenfeld's Bacteriology.)

T. pallidum in nature attacks only human beings, but apes and rabbits can be experimentally infected.

The Disease. — Syphilis is a disease which has no equal in its deceptive nature. It is largely due to this fact that so many tragedies result from its ravages. Its effects on the individual are often horrible enough, leading to disease of almost any tissue or organ in the body, but it is only when judged in the light of the additional damage that is done to the innocent wife or husband, as the case may be, and to the next generation, that the true meaning of syphilis can be measured. Syphilis may remain latent and unsuspected for twenty years or more, and the carrier still be infective. Meanwhile, perhaps in ignorance of his condition, he may infect a hitherto sound person whom he has taken for a life companion, and cause her, or him, to be ravaged and slowly destroyed by this horrible disease. Worse than this his chances of having healthy children are small. It has been shown that about 45 per cent of those who later become victims of general paralysis from syphilis never can have any children, either on account of sterility or of repeated abortions. The author of the statement in the Bible that "the sins of the fathers shall be visited upon the heads of the children unto the third and fourth generations" may well have had in mind the hereditary effects of venereal diseases, but he might have stated further that often there is no third or fourth generation. The only pity of it is that this is not always the case, for those who are brought into the world are in the majority of cases hopelessly handicapped either mentally or physically. Feeble-mindedness is five times as common in syphilitic families as in normal ones. There is some reason for believing that the hideous mentally deficient children known as mongols are the result of syphilis in parents. And finally, as if all this were not enough, the carrier of latent syphilis may later develop general paralysis, or some other disease of the nervous system or other organs, which will render him an ineffectual social unit, and make him and his family a burden to the community.

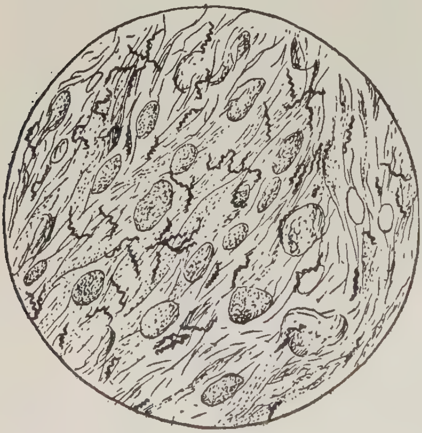
FIG. 10. *Treponema pallidum* in liver tissue of a congenital syphilitic.

In the majority of cases the disease begins with a hard sore on the skin or mucous membrane known as the "primary chancre." This usually appears at the point of infection in from ten days to six weeks, usually about four, after the infection occurs. The chancre gradually heals up and the second stage begins, in which constitutional symptoms appear, such as fever, anemia and a general run-down condition during which the patient is very susceptible to other diseases, such as tuberculosis. Often there is an extensive breaking out on the body, production of scaly patches of skin, and inflammation of the mucous membranes of the mouth and throat. Headache, rheumatic pains and enlarged glands are common.

Following the secondary stage there is usually an " early latent period " lasting several months to many years, usually two to three years, before the deeper lesions become prominent. Often there is a revival of the secondary symptoms before the appearance of the tertiary ones.

From this point on the course of the disease depends on what particular tissues or organs the spirochætes especially attack, for although the parasites, as said before, may produce disease almost anywhere in the body, in any given case there is usually a localization. It seems that certain strains of the parasites have special preference for certain tissues. The differences in this respect have been shown by Nichols to hold good through many transfers from animal to animal, and visible differences in the parasites have been claimed. In about 40 per cent of cases in temperate climates syphilis settles in the nervous system, causing a great variety of evil effects, such as feeble-mindedness, tabes, or locomotor ataxia, general paralysis, epilepsy, insanity and moral defectiveness. In tropical natives, on the other hand, neuro-syphilis is practically unknown; it has been suggested that this may be due to malaria or other fevers, which have been shown to have curative effects on syphilis of the central nervous system. Syphilis often settles in the skin and mucous membranes, producing the gummy sores or " gummas " which were formerly supposed to be the usual tertiary stage of syphilis. It may select the bones, muscles, arteries, heart, reproductive system, or any other part of the body, in each case producing a different set of symptoms, but in every case weakening the vitality and leading ultimately to an early grave.

An active attack on one tissue or organ of the body seems to have an inhibiting effect on other attacks. It is well known that an infected person presumably with an active attack of the spirochætes on some organ in his body will not develop new lesions when re-infected. Possibly this explains why there is often a relapse of the nervous system after incomplete treatment of skin syphilis. The spirochætes in the nervous system which are not reached by the drugs may flare up and produce a serious attack after the spirochætes in other parts of the body have been killed and the skin lesions healed. On the other hand paralytics with an active attack on the central nervous system seldom show any other symptoms. Unborn babies seem not to be subject to such specialized attacks, but, as already pointed out, are often found with every organ and tissue in the body full of spirochætes. There is a form of the disease occurring in adults known as " malignant syphilis " in which ulcerating sores appear early and gradually eat away large portions of the skin. It is marked by extreme anemia and great weakness, and usually causes an early death.

Diagnosis. — The modern methods of diagnosing syphilitic infection have revolutionized our knowledge of the disease, and have done much toward placing its treatment and control on a scientific basis. In at least 50 per cent of late syphilitic cases there are no symptoms which can be attributed positively to syphilis, but we now have tests which make it possible to detect syphilis in practically any phase. In the chancre stage examination of expressed serum for spirochætes, under a dark-field microscope, is very reliable and much better than any of the staining methods; of the latter the Fontana stain is the best. Often spirochætes can be demonstrated, on a dark field, in material obtained from puncture of an enlarged lymph gland.

The Wasserman reaction, although not infallible, is one of the most valuable and dependable means of diagnosis known in medicine. If repeated, it gives a high percentage of positives even within a week or two of the appearance of the chancre, and in later stages it positively diagnoses the great majority of cases. The test is also positive in yaws, which is doubtfully distinct from syphilis, and in relapsing fever, and is occasionally positive in cases of malaria, leprosy, and a few other diseased conditions. The test depends on the fact that the serum is so altered by a syphilitic infection that the " complement " of fresh blood is fixed or absorbed in its presence by a lipoidal substance which is called the antigen. This fixation of the complement is then tested for by adding to the serum a suspension of blood corpuscles, and specific antibodies for the corpuscles in the form of a hemolytic serum. If the complement is still present, as it should be if the person tested is not syphilitic, the sensitized corpuscles are dissolved, whereas if the complement has been fixed by syphilitic serum the corpuscles remain intact. A substitute for the Wasserman test, the Kahn test, has come into much favor recently; in this case the test depends on the fact that a certain dilution of the antigen in salt solution will form a precipitate which is redissolved on addition of normal serum but not on addition of syphilitic serum. This test is much simpler than the Wasserman and apparently just as reliable. In either case the test requires skill and experience before the results can be considered dependable.

Treatment. — There are many quack doctors who are still practicing the same inefficient methods of curing syphilis that were in vogue several centuries ago. Syphilitic sores are powdered and cauterized and cured, and the patient is given to believe that his disease is cured. Unfortunately, as we have seen, the course of the disease is of such a nature that the doctor's claim of having cured may be borne out for months or years before the insidious disease appears again, this time in a much more destructive and perhaps incurable state. Superficial treatment of syphilis sores, accompanied perhaps by a few " tonic " pills, in no way destroys the virulence of the parasites or alters the future course of the disease. It merely makes the chance of correctly diagnosing the disease more difficult, and it frequently results in an unsuspecting victim carrying the disease untreated to a stage where it has wrought irreparable damage to himself, his life-mate and his children.

Treatment of the disease formerly consisted in the administration of mercuric chloride. While this sometimes effected an apparently complete cure, over 80 per cent of syphilitics suffered relapses in spite of the most persistent treatment. In 1910 Ehrlich, after years of experimentation, offered humanity his famous preparation, " No. 606," which he named salvarsan; it is an arsenic compound chemically known as arsphenamine, which has a deadly effect on spirochætes in the body of a patient. When this drug is injected into the veins of a syphilitic, it almost immediately kills all the spirochætes except a few which have stowed away in inaccessible parts of the body, and these must be caught by continued administration of the drug, or by special methods. There are now on the market many modified forms of arsphenamine, such as neosalvarsan, sulpharsphenamine, etc., about the relative virtues of which opinions differ.

Intravenous injections of arsphenamine do not reach the spirochætes in the central nervous system. Since it is too injurious to be injected directly into the spinal fluid, a modified treatment first devised by Swift and Ellis in 1913 is used; the drug is first injected into the blood, and an hour later some serum is withdrawn and injected into the spinal canal in diluted form. Very good results have been obtained by the use of this " auto-salvarsanized serum." In recent years, syphilitic general paralysis has been treated by artificially inducing fever, usually by the deliberate infection of the patient with benign tertian malaria, or sometimes relapsing fever, and some excellent results have been obtained. The immediate effects are striking, and a fair percentage of cases seem to be permanently cured.

The alternate use of mercury and arsphenamine seems often to be more effective than either one alone. In recent years much further work has been done on spirochæticidal drugs. In 1921 it was demonstrated that bismuth is more effective than mercury in its action on spirochætes, and is less toxic to the host. Levaditi and his colleagues have shown that very minute quantities of bismuth are required to cause the destruction of spirochætes; mere traces of the metal seem in some way to stimulate the natural powers of the host in its combat with the invading organisms. Gold and other related metals have similar effects. Insoluble bismuth compounds, when injected into the muscles, are slowly rendered soluble in the tissues and supplied to the body in minute quantities sufficient to kill the spirochætes. As with mercury, alternate injections of bismuth and arsphenamine, or the latter followed by the former, may give better results than either drug alone.

The modern methods of diagnosing syphilitic infection have given a definite standard of cure, and the success or failure of treatment can be positively demonstrated. A uniform negative Wassermann reaction given several times during a year, and absence of any symptoms, can be looked upon as an indication of cure, though some doctors consider a negative Wassermann reaction for two years necessary to indicate a certain cure on account of rare cases of relapse, even after a year of apparent absence of the spirochætes. In contrast to the 80 per cent of relapses which occurred when mercury alone was used to treat syphilis, less than four per cent of relapses occur after treatment with both mercury or bismuth and arsphenamine. Certainly arsphenamine may justifiably be considered " one of the mightiest weapons in medicine."

Prevention. — The control and ultimate eradication of syphilis is, in spite of our present methods of diagnosis and treatment, a dream of the distant future. In its prevention are involved so many social and moral problems upon which people will not agree that the task is beset with great difficulties.

According to Dr. Snow of the American Social Hygiene Association, the means of controlling and preventing syphilis fall into three groups: (1) care and treatment of existing cases with a view to preventing their spreading the infection, (2) protection of the uninfected by education and administrative measures, (3) the development of social defenses against the disease.

As regards the first type of preventive measures, practically all medical men and public health workers are agreed. Adequate means for the diagnosis and treatment of syphilis should be provided in all cases. Much improvement in this respect has been made in recent years. A few years ago not only were there no laboratories for diagnosis or free hospitals or clinics for treatment provided at public expense, but most of our private physicians and hospitals shunned syphilitics, and refused to care for them. There are very few cities now which do not provide facilities for diagnosis and treatment. Unfortunately many general practitioners know far too little about venereal diseases, and insufficient emphasis is placed on them in many medical schools. Theoretically syphilitics are dangerous sources of infection, and as such should be kept under observation and not turned loose without treatment or control, with full power to infect others. Such a procedure is no advance over the attitude displayed in 1496, when the Parliament of Paris decreed that all persons found infected with syphilis should leave the city within 24 hours. Not only can most cases of syphilis, if reached early, be cured, but medical prevention of syphilitic infection after exposure to it is possible, and succeeds in the great majority of instances if attended to within a few hours after exposure. The use of self-applied medical treatments has been fairly successful in military life, but as shown by Snow it is of doubtful value in civil life, since the intelligence required to apply medical preparations properly is lacking in those who need it most, — immature boys, drink-befuddled men, defective girls, and the average prostitutes. These classes constitute the bulk of the citizens who become exposed to infection, and since the personal supervision of a physician is necessary in most cases, it might best be required in all. Private physicians, dispensary officers and the health department staff are the persons qualified to employ medical treatment designed to prevent infection *after* exposure to it. Avoidance of exposure constitutes the best and only safe preventive measure *before* exposure.

As to the second type of prevention, the protection of the uninfected by education and administrative measures, great advances are being made. One of the most important measures, and one to which we are slowly coming, is the compulsory notification of the Public Health Department of all cases of venereal diseases so that whatever action seems best may be taken to safeguard the public health. There can be no question but that such a recording of venereal diseases would work for the best good of all concerned, both the patient and the public. Laws compelling the notification of health departments of venereal diseases now exist in most states in the United States, but in more cases than otherwise they are not enforced.

With the notification of venereal diseases, many other practical measures could be inaugurated, such as the exclusion of infectious syphilitics from occupations connected with the preparation and serving of food; the careful instruction of syphilitics concerning various phases of their disease, and possible means of transmission, thus in many cases securing their active coöperation; and the effective prevention of the marriage of syphilitics. The last is one of the most important measures that could be adopted. Many states at present prohibit the marriage of persons with venereal diseases, but without enforcement of notification these laws are worse than useless, since they may give a false sense of security. Knowing the awful consequences of inherited syphilis it is the duty of society to prevent the marriage of syphilitics even with the full knowledge and consent of both parties. The Royal Commission urged only the full information of the undiseased party in marriage, allowing the union to be made if then consented to. In this they seem not to have given due consideration to the rights of the next generation. With compulsory notification of venereal diseases, and a law refusing a marriage license to any person who has or has had syphilis and cannot pass the accepted laboratory tests for the disease, the pitiful results of hereditary syphilis could be largely prevented. Even the remote possibility of the spectacle of a diseased wife and of still-born, insane, or physically imperfect children should be enough to induce any man worthy of the name to take every precaution to avoid such a tragedy, but if he is unwilling to do this for himself and his posterity, social laws should do it for him.

Sanitary laws are in effect in many places which help to prevent infection from such sources as public drinking cups, towels, bed-linen, and other articles, but such laws, excellent as far as they go, are inadequate, since no law can cover all the articles which may be rendered infective by contact with a syphilis sore. One common source of infection, though more for gonorrhea than for syphilis, is the improperly constructed toilets in public schools. These are usually built so high and of such a type that school children, little girls especially, are exposed to infection every time they use them. Many cases of venereal diseases in school children, particularly in larger cities, have been traced to this source.

No preventive measure which does not strike directly at the primary source of infection can be adequate in coping with any disease. Just as we fight malaria through the mosquito, sleeping sickness through tsetse flies and typhoid through contaminated water and houseflies, so we must fight syphilis and other venereal diseases through prostitution. The abolishment of this vice would soon lead to the abolition of venereal diseases. At present, at least in many places, this is certainly not possible. The abolition of "red light" districts is invariably followed by a parallel increase in clandestine prostitution, luring many who would abstain from unmasked brothels, to say nothing of the increase in seduction and rape of innocent girls. A plan successfully tried in many European cities, especially Germany, is the municipal supervision of restricted "red light" districts. By continuous medical attendance, and the enforcement of strict sanitary measures, the normal spread of disease from this source has been reduced to a great extent. It may be argued that municipal control of prostitution implies public sanction of it, and is therefore morally wrong. This perhaps is true but there can be no question about the futility of attempting, at the present state of our civilization, to abolish prostitution or even to lessen it materially by passing laws against it. In view of this it is merely a question of a greater or lesser evil, and there can be no moral crime in lessening the dangers from an evil which we are powerless to destroy. It may be said that the lessening of danger from disease in houses of prostitution will increase their popularity. The same argument might be used, and has been used by the ultramoralists, to show that it is morally wrong to attempt to cure venereal diseases, since this lessens the terror of them. Such arguments might have more force if syphilis were a disease which affects only the individual, and was not a source of danger and burden to the community. Moreover it seems doubtful whether the person whose character is such a combination of moral weakness and cowardice that he shuns houses of prostitution only from dread of disease, will not spend his time in seducing innocent girls, or in other hardly less despicable crimes. It may further be pointed out that disease and immorality go hand in hand. A healthy body is conducive to a healthy mind, so by eliminating disease we would be doing at least as much toward giving a death stab to immorality as toward extending it.

The medical supervision of prostitution, adopted as a temporary measure, should be accompanied by efforts toward its ultimate reduction. The abolition of alcoholic drinks, the improvement of conditions in slums, the furnishing of decent surroundings and wholesome sports and exercises, and the enforcement of minimum wage laws for women are all measures which tend toward the reduction of prostitution, but foremost of all such measures should be education; in this lies our most powerful weapon against immorality and venereal disease. Hospitals, public schools, churches, libraries and the lecture platform all have the power of spreading the gospel of sex hygiene, each in its own way, each in a way especially suited to its listeners. The freer modern attitude toward sex topics, though deplored by some, will probably result in much more good than harm.

Yaws

A common feature of nearly all tropical countries is the disease known as yaws or frambesia. In the Fiji Islands all healthy children are expected to pass through an attack of yaws and are sometimes inoculated with it by their parents. It is common in many parts of equatorial Africa, particularly on the West Coast. In the West Indies it is also a very common disease, especially in the islands which are largely inhabited by negroes. There is some evidence that yaws was imported to

America from Africa with the slaves as were some others of the most troublesome American diseases. In Brazil the disease is called " buba brasiliensis " and is often confused with Leishmanian diseases.

The spirochæte which is the cause of yaws was discovered by Castellani (1905) in the same year that Schaudinn discovered the spirochæte of syphilis; it is known as *Treponema pertenue.* Morphologically it is impossible to distinguish this organism from *T. pallidum* of syphilis, although Knowles considers it slightly more flexible. There has been unending discussion as to whether yaws is a separate disease entity, or is a form of syphilis modified by climate and race, and adapted to contagious instead of venereal transmission. The parasites are certainly very nearly related both morphologically and biologically; to some extent, at least, the two diseases produce immunity to each other, and the general nature of the infections to which they give rise is strikingly similar. Clinically, however, there are numerous differences, the geographical distribution is different, and the mode of transmission is different. Whether or not yaws was originally evolved from syphilis or vice versa, or whether under suitable conditions the alteration can still occur, is largely an academic question. Practically, yaws is a recognizably distinct disease. *Treponema pertenue* produces somewhat different lesions in rabbits than does *T. pallidum.* The fact that syphilis and yaws are never both prevalent in one locality is undoubtedly due to the reciprocal immunity conferred by these diseases for each other.

The Disease. — In from 12 to 20 days and occasionally longer after infection constitutional symptoms appear, such as fever, rheumatic pains and general illness. These symptoms are sometimes very severe, but usually they are slight and often hardly noticeable. A primary lesion, corresponding to the chancre of syphilis, may or may not occur, but it is always inconspicuous, usually in the form of a papule. After several days of such symptoms there appears a peculiar powdery scaling-off of the skin, sometimes almost invisible but at other times making white marks, especially conspicuous on the dark skin of negroes. After several days little pimples appear over the hair follicles in the patches of powdery skin. As these grow the raw flesh from beneath pushes the horny epidermis up, causing it to crack over the surface in such a way as to give the little tumor the appearance of a raspberry. Little yellow summits soon develop on the tumors, composed not of pus but of a cheesy material. Some of the pimples grow no further, but most of them become capped over with the yellow cheesy substance which catches and holds particles of dust, and thus becomes very dirty. These are the " yaws " from which the disease takes its name. During their formation they cause some itching, but are not painful. They reach the height of their development in 12 or 14 days and then usually begin to shrink, the dirty yellow cap, now dark colored, falling off and leaving a sound patch of pale skin. Sometimes, however, though in less than 10 per cent of cases, ulceration of the yaws takes place, but this is probably due to complicating infections. The time that the disease lasts varies greatly according to the general health and constitution of the patient. In normal mild cases it may be all over in less than two months, while in weak or sickly individuals crop after crop of yaws may appear for months or years, recurring at irregular intervals. Tertiary lesions of skin, joints and bones occur sometimes, either with, or long years after, the yaws stage. There is good evidence that the central nervous system and eyes are never attacked, and the mucous membranes rarely if ever. Probably many supposed late manifestations of yaws are really due to syphilis, for a differentiation in late stages can be made only on the basis of the early history of the case. A disease known as gangosa, prevalent in many places in both the East and West Indies, causing a horrible ulceration of the entire nose and palate area, is thought by some observers to be due to yaws. Yaws is very seldom a fatal disease except in young children. Although it is is very contagious, the parasites are not transmitted from mother to baby before birth or by nursing.

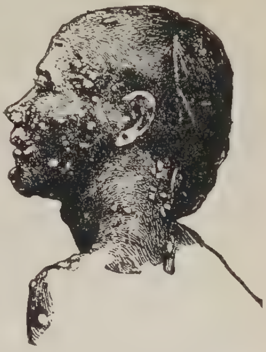

Fig. 11. A case of yaws. (After Manson.)

Yaws is spread by contagion, no doubt often by either biting or non-biting flies, but the spirochætes always enter through some abrasion of the skin, such as ground itch from hookworm, leech or insect bites, scabies, vaccination wounds, scratches, etc. Gonzaga, in Brazil, believes that *Culicoides* act as agents in transmission. In Samoa the disease becomes epidemic following the season when flies are most abundant. In Assam there is a belief that the " eye-fly," which abrades the skin with its mandibles, transmits the infection.

Treatment and Prevention. — Care of the general health of yaws patients and conditions leading to the free eruption of the yaws aid much in shortening and alleviating the course of the disease. The spirochætes are affected by arsphenamine and its derivatives more readily than in syphilis, and in many cases one, and in the majority two or three, injections effect a cure. Excellent results have also been reported from a course of treatment with another arsenic compound, stovarsol, which can be given by mouth. Bismuth treatment is also giving good results, but yaws is much more refractory to mercury than is syphilis.

The suppression of yaws in communities where it is common consists largely in affording isolated hospitals or houses for yaws patients and in preventing the patients by proper care and treatment from spreading the disease by contagion. Personal care on the part of the patient is often more than could be expected, considering that yaws is most common among half-civilized and ignorant tropical races. However, the lure of a comfortable and congenial ward where he could get good treatment would undoubtedly induce many a native to submit to the practice of being sanitary, however it might grate upon his nerves at first. His accounts of the good treatment received would help in luring others, and what few ideas of sanitation he might have retained would help in spreading the gospel of sanitation. In this way the prevalence of the disease, at least in local areas, could be greatly reduced, and public money used for such purposes could be considered well spent.

Treatment campaigns, using one or two injections of some effective drug to reduce the number of actively contagious cases, rather than to effect complete cures, are being tried, but there is danger that there may be a great increase in number of latent and tertiary cases.

Spirochætes in Local Infections

Spirochætes occur so commonly in different parts of the body of man and animals, and their separation into species is so uncertain, that our present knowledge of the relationships and pathogenic powers of these various spirochætes is in a terrible muddle. Some observers, finding spirochætes present in an infection or lesion, conclude forthwith that they are the cause of the condition. In some instances there is reason to believe that the spirochætes may really be at least in part responsible for the infection, or may aggravate it by their presence, but in other cases even this is doubtful. Fifty or more different spirochætes, recovered from inflamed or diseased tissues, have been described, yet it is doubtful if any single one of them could be identified apart from the lesion with which it is associated.

Saprophytic spirochætes of several types occur very commonly in the human mouth. There is a large one with coarse spirals resembling *T. recurrentis*, named *T. buccale;* one which closely resembles *T. pallidum* and is called *T. dentium* or *microdentium;* and a number of other intermediate types. A similar variety of types occur in the intestine, but have been given different names. One of the commonest saprophytic spirochætes is *T. refringens*, characterized by its brilliant refringent appearance under dark-field examination. It is common in the mouth, mucous membranes, genitals, and often in association with *T. pallidum* in syphilitic lesions. Whether or not these apparently harmless spirochætes, so often present in entirely normal individuals, are identical with the spirochætes which secondarily invade diseased tissues, and perhaps aggravate them, it is impossible to say.

Vincent's Disease, Tropical Ulcer, etc. — One of the most important of these secondarily developing conditions is Vincent's disease, which appears to be caused by two entirely different organisms living in a symbiotic partnership, one a spirochæte which has been named *T. vincenti*, and the other a large, cigar-shaped, fusiform bacillus. It affects either mucous membranes or subcutaneous tissue; in the throat it usually follows a streptococcus infection and causes a diphtheria-like ulceration of the tonsils and throat which is known as Vincent's angina; in the skin it produces lesions which are called tropical ulcers, or by the more impressive name, tropical sloughing phagedæna. These sores originate either in some slight abrasion of the skin or in some pre-existing wound or sore, most commonly on the feet or legs, especially in persons debilitated by some other disease or by alcohol. Beginning as a tiny blister there develops a nasty sloughing ulcer which may spread over a large area, but eventually usually heals. A severe and very common form of the infection occurs in Assam, known as Naga sore; the gangrenous process erodes tendons, muscles and even bone, and a horrible, yellowish slough is formed which has a characteristic fetid odor. In all of these cases the spirochæte and fusiform bacillus occur together, although deep in the tissues only the spirochætes are found. The tropical ulcer spirochætes, in stained preparations, are 12 to 25 μ in length, very slender, with loose open coils, 6 or 7 to every 10 μ. They have been named *T. schaudinni*, but are very likely identical with *T. vincenti*, and possibly even with *T. buccale* of the mouth. It is not certain that these spirochætes are really pathogenic, though in this case it appears likely. Arsenic compounds usu-

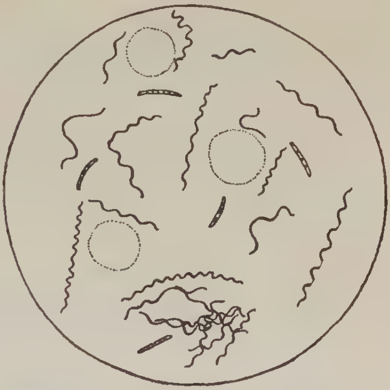

FIG. 12. Spirochætes and fusiform bacilli in a smear from a tropical ulcer. × 1000. (After Wenyon, "Protozoölogy.")

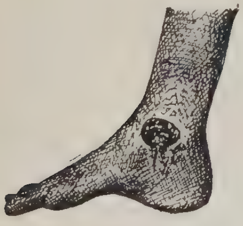

FIG. 13. Tropical ulcer (Drawn from photo by Halberstadter in Kolle and Wassermann.)

ally have a beneficial effect, and applications of potassium permanganate are said to bring good results. Vincent's angina is treated by local applications of arsphenamine or silver nitrate; the latter is less dangerous and just as efficacious for these superficial ulcers. A different type of skin lesion of the foot and ankle, in which large masses of granulation tissue is formed, has been described from South America by Strong and his colleagues; a spirochæte found associated with it, and believed to be the cause, was named *T. noguchii.* This may possibly be related to ulcerating or inguinal granuloma, a sore which slowly spreads in the genital region, and in which spirochætes are often found. In this case, however, the infection is now believed to be due to certain types of bacteria and not to spirochætes.

Mal-de-boca (disease of the mouth) in Central America; noma, an ulceration of the mouth cavity and cheeks; balanitis, an ulceration of the genital organs which may occur after unnatural sexual relations; and other ulcerative conditions are all characterized by the presence of spirochætes and fusiform bacilli in partnership. At present one can only speculate as to the relationships of these various spirochætes, and bacilli, to each other, and to those found in normal mouths and mucous membranes. The presence of heat, moisture, filth and absence of air seem to favor the development of the organisms in lesions.

Bronchial Spirochætosis. — Another very widespread condition in which spirochætes are involved is a disease of the lungs, first described by Castellani in 1905, and usually called bronchial spirochætosis. The disease is characterized by the presence of abundant spirochætes, which have been named *T. bronchiale, without* fusiform bacilli associated with them. The outstanding symptoms are a constant cough, abundant frothy and sometimes blood-stained sputum, pain in the chest, and sometimes, in chronic cases, pulmonary hemorrhages. In a majority of cases the spirochætal infection seems to follow tuberculosis or some other lung infection, but many observers have reported uncomplicated cases. The spirochætes are described as being very variable in size and form, and can certainly not be identified by any available descriptions of them. Fantham has described the formation of granules by these spirochætes, as in the case of *T. recurrentis*, and thinks the infection may be spread by the granules as well as by the spirochætes themselves. Dobell thinks *T. bronchiale* is identical with *T. buccale*, while Vincent and others identify it with *T. vincenti*, from which, however, it differs in not being accompanied by fusiform bacilli. Tunicliff believes that the spirochætes and fusiform bacilli are different forms of the same organism, and claims to have seen spirochætes develop from granules in the bacilli, but there has been no confirmation of this remarkable process by other workers. Wenyon and some others are very skeptical of the pathogenic nature of the spirochætes; Wenyon thinks it would be as logical to consider every mouth abnormality as due to mouth spirochætes when these can be found there, as to accuse the bronchial spirochætes of being the cause of the diverse pulmonary disorders in which they have been found present. The fact, however, that in acute uncomplicated cases immediate relief, accompanied by a disappearance of the spirochætes, is effected by injections of arsphenamine and other spirochæticidal drugs is hard to explain if the spirochætes are mere saprophytic invaders without pathogenic power.

Infectious Jaundice and Other Leptospira Diseases

The genus *Leptospira* contains extremely delicate spirochætes in which the body consists of a very fine filament with tapered ends, so closely and regularly coiled as to resemble a rope (Fig. 14). They are very active, and often have the ends of the body hooked over in a characteristic manner; other spirochætes, it should be recalled, tend to keep the bodies extended in a straight line while swimming. When examined with a dark-field microscope the leptospiras look like little brilliantly refractile swimming bits of rope, but after being dried and stained the fine rope-like coils are usually not visible, and the organisms appear like tiny threads with hooked or looped ends.

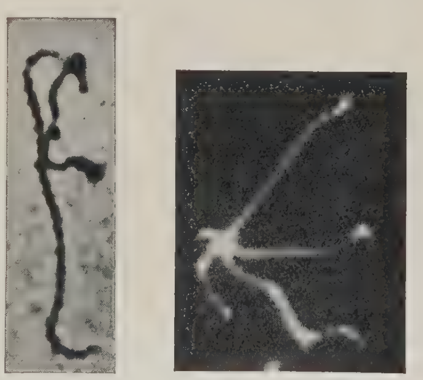

Fig. 14. Microphotographs of *Leptospira icterohæmorrhagiæ;* at left, a stained specimen; at right, three living specimens as seen under dark-field examination. (After Noguchi in Journ. Exp. Med.)

There is at present much doubt about the relationship of different strains of *Leptospira* which have been obtained from cases of infectious jaundice and related diseases of man or rodents, and free-living forms which are common in water in all parts of the world. The latter occur especially in slimy growths in water, particularly when the nitrogen content is high, and are even found in the sea.

In 1921 Noguchi isolated a *Leptospira* from the blood of a number of cases of true or supposed yellow fever in South America, and concluded, with much justification, that this organism, which he named *L. icteroides*, was the cause of yellow fever. Subsequent work has failed to confirm the presence of leptospiras in uncomplicated and unquestionable yellow fever either in South America or Africa, and extensive immunological work by Sellards and Theiler, and many others, has left no room for doubt but that this organism is identical with the leptospira which has been shown to be the cause of infectious jaundice or Weil's disease, and which is known by the mouth-filling name, *Leptospira icterohæmorrhagiæ.* Closely related spirochætes have been shown to be the cause of Japanese seven-day fever and Japanese autumnal fever. Couvy and a few others have described leptospiras from the blood of dengue cases (see p. 197) and claim to have recovered the organism from experimentally infected animals, but very extensive and careful work by others have failed to corroborate this. Likewise Whittingham has isolated a leptospira from cases of sandfly fever, but this organism did not produce sandfly fever in susceptible persons.

Infectious Jaundice. — This disease, which is now known to occur sporadically or in local epidemics in all parts of the world, was shown in 1915 by two Japanese workers, Inada and Ido, to be caused by a leptospira, to which they gave the species name *icterohæmmorhagiæ.* Later in the same year the same organism was discovered by German workers in cases of Weil's disease, which is the same as infectious jaundice. They suggested the name *nodosa.* One might wish that the Germans had named the spirochæte a few months earlier! The disease begins suddenly with headache, chills, vomiting, diarrhea, etc., soon followed by a fever and a feeling of leaden fatigue in the legs, which later changes to a severe aching and painfulness to touch. Usually jaundice develops after a few days, and small hemorrhages may appear in the skin and mucous membranes and in internal organs. The fever subsides about the tenth day, but may reappear at intervals. The jaundice may be severe or very slight; the urine nearly always contains both bile and albumen.

The spirochætes are usually demonstrable in the blood towards the end of the second week, but are more easily found in the urine after centrifuging. They vary in length from about 5 to 25 μ, and have the characteristic hooked ends. According to Noguchi there are 10 to 12 coils in 5 μ of the length. As shown in experimental animals, the leptospiras attack particularly the liver and kidneys, and the outstanding symptoms are jaundice, extensive internal hemorrhages, and albuminuria. Guinea pigs are very susceptible, and usually die; they can be infected by injection of blood in early stages of the disease, or of urine later. Rats are less seriously affected, and usually get chronic infections. A high percentage of wild rats in many places have been found to harbor the leptospiras, which occur particularly in the kidneys and are excreted with the urine; they are most easily demonstrated by inoculating an emulsion of the kidney into guinea pigs. It is generally conceded that rats are an important reservoir of the leptospira, but just how transmission to man occurs is uncertain. During the great war it was supposed that soldiers became infected through abrasions of the feet contaminated by the dead bodies or urine of infected rats, or by contamination of food or drink by excretions of these rodents. In some cases, however, water used for drinking or bathing seems to be more intimately connected with the epidemiology than rats, and it is possible that infection may occur by pollution of water by human urine, directly or indirectly. Since guinea pigs can be infected directly through the unbroken skin, it is possible that no abrasion is necessary, and contact of skin or mucous membranes with infective material may be sufficient.

In Sumatra there occurs a mild form of the disease characterized by a short dengue-like fever of two to four days' duration, followed by a few days of normal temperature, and then one or two, occasionally up to five, progressively shorter and milder relapses. The leptospira involved has been called *L. pyrogenes.* Baermann and Smits believe the infection is derived from water while bathing, which would account for the high proportion of cases in males.

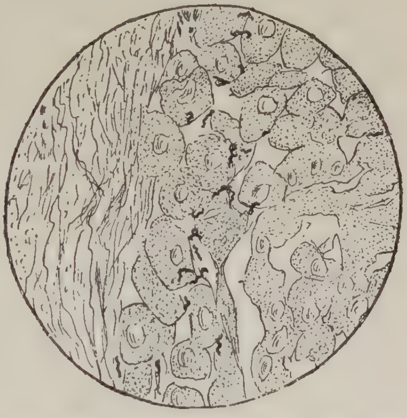

FIG. 15. Liver of patient who died from Weil's disease on sixth day, showing *Leptospira icterohæmorrhagiæ* in tissue. × 200. (Sketched from figure by Inada et al.)

In Germany also there is a modified type of Weil's disease which has been called "slime fever," since it seems to be derived from bathing in stagnant water containing slimy growths.

In Japan there are two other diseases which have been shown to be caused by leptospiras, as well as infectious jaundice; they differ in that jaundice is of rare occurrence. The leptospiras are morphologically indistinguishable from *L. icterohæmorrhagiæ.* One of these diseases, called seven-day fever, has a fairly wide distribution among Japanese field workers. The organism involved is named *L. hebdomadis;* serum immune to this spirochæte either fails to agglutinate *L. icterohæmorrhagiæ,* or does so only in relatively low dilution. An organism believed to be identical with this has been found in the Japanese field mouse, *Microtus montebelloi*, and the Japanese believe that this mouse acts as a reservoir for the disease, as the rat does for infectious jaundice. Another similar disease in Japan is called autumnal fever; two different strains of leptospiras have been isolated from cases of this disease; one, called *Leptospira autumnalis* A, produces jaundice in guinea pigs similar to that caused by *L. icterohæmorrhagiæ*, and on prolonged culture becomes immunologically closer to the latter form; the other, called *L. autumnalis* B, seems to be immunologically distinct from A, but identical with *L. hebdomadis*.

One thing seems clear enough, that the relationship of the various leptospiras of disease in man and rodents, and of those found free-living in water, is at present not clear at all. Practically all modern workers agree that *L. icterohæmorrhagiæ* and *L. icteroides*, which Noguchi connected with yellow fever, are identical; that the immunological reactions by the various strains, either from animals or water, are subject to alteration as the result of cultivation and passage through animals; and that the water strains can, under certain conditions, become parasitic and pathogenic. Baermann and Zuelzer produced a mild infection in a woman by a water leptospira which they had cultivated. A guinea pig was inoculated from the woman, and a second guinea pig from the first one. The woman's serum then actively agglutinated the original water strain but had no effect on the same organisms after passage through two guinea pigs! Not all strains of typical infectious jaundice are alike. *L. hebdomadis* immune serum agglutinated 7 strains from such cases but had no effect on 129 others. Baermann and Zuelzer are inclined to look upon all the leptospiras, parasitic or free-living, as one species, capable of modification in pathogenicity and immune reactions as the result of passage through animals. The clinical symptoms produced presumably depend on the quantity of the infective dose, on variations in virulence dependent on whether the organism has recently lived a parasitic or free life, and on the constitution and temporary state of health of the infected animal or man.

CHAPTER V

AMEBÆ

Those of us who have had an opportunity, in studying microscopic life in water, to observe the restless movements of the tiny bits of naked protoplasm which we call amebæ, having watched them slowly creep along the surface of a slide, extending a portion of the body as a finger-like projection or " pseudopodium " and then allowing the rest of the body to flow up to the new position; having seen them creep up on tiny protozoans or other single-celled organisms and devour them by merely wrapping themselves around them, thus engulfing them in an improvised stomach; and having seen them propagate their kind by simply constricting in the middle and dividing in two; — those of us who have observed these acts on the part of such tiny and simple animals have come to be fascinated by them and to like them, and find it hard to realize that certain species are instrumental in causing some important human diseases. Amebæ are found almost everywhere in water, soil and carrion. They have even been found to exist in large numbers in the sun-baked sands of the Egyptian deserts, lying dormant in their cysts which protect them from evaporation, ready to emerge and resume an active life when they become moistened. In view of the wide adaptability of these animals it is not surprising to discover some living as parasites, finding congenial surroundings in the bodies of higher animals.

Classification. — Amebæ are protozoans belonging to the class Rhizopoda (or Sarcodina), a group characterized by a body without a cuticle, though sometimes protected by a shell or cyst wall, and by their peculiar method of locomotion. In the adult form they have neither flagella nor cilia, but only pseudopodia. In the amebæ and their close relatives the pseudopodia can be projected anywhere on the surface of the body, now here, now there, though the number, form and activity of the pseudopodia are quite different in different species. The life history also varies in the different species, many free-living forms possessing a flagellated stage. On the basis of structure, life history, type of nuclear division, and habits the old genus *Amœba* has been broken into a number of genera distinguishable from each other principally by the structure of the nucleus and the nature of the cysts. The life history is simple in all of them, so far as it is known. The cases of spore formation, multiple fission, conjugation or sexual processes described by various investigators have not been substantiated by subsequent work. All of the parasitic amebæ are characterized by the absence of contractile vacuoles. One species, *Endamœba histolytica*, habitually feeds on blood corpuscles and living tissues, and is definitely pathogenic, while others rarely if ~~ever do so, and most~~ of them, at least, may be considered entirely harmless commensals which live peacefully in the intestines of their hosts and feed on bacteria and other organic material with which they are associated. In addition to these true inhabitants of the intestine there are others which are spoken of as coprozoic, *i.e.*, they commonly live and multiply in feces, having gotten access to them by being accidentally ingested with food or water in the form of cysts, which " hatch " and multiply after passing through the digestive tract unharmed. In addition to various forms of free-living amebæ, all distinguishable from the truly " entozoic " forms by their contractile vacuoles, there is also a shelled organism, *Chlamydophrys stercorea*, sometimes found in stale human stools, though more commonly in stools of pigs and horses. There is no evidence that any of these coprozoic forms can ever establish themselves and multiply in the intestines; they become progressively more abundant in stale feces, whereas the active stages of the true intestinal species die out very rapidly and leave only cysts after a few hours.

There is still a difference of opinion as to the number of species of amebæ which habitually live in the human body, and to the relationship of these forms to those in other animals. Prior to the publication, in 1919, of Dobell's book on " Amœbæ Living in Man," the human amebæ were in a terrible muddle, and most of the earlier literature cannot be relied on so far as species are concerned. Since the publication of this valuable work there has, perhaps, been some tendency to accept it too much as a " Bible," and to regard modifications and additions as more or less heretical. All protozoölogists at present recognize the following genera and species: *Endamœba gingivalis*, in the mouth; *E. histolytica*, the only species known to be pathogenic; *E. coli; Endolimax nana; Iodamœba williamsi* (= *bütschlii*); and *Dientamœba fragilis*, a rare form. In addition to these there are a number of other species which, although not accepted by many protozoölogists, and therefore still *sub judice*, nevertheless appear to have strong claims for recognition, and hardly to deserve the incredulity with which they have been received. The most important of these are three species which Kofoid and his colleagues place in a separate genus *Councilmania*, namely *C. lafleuri*, *C. tenuis* and *C. dissimilis*, and a quite different form, *Karyamœbina falcata*, described by Kofoid and Swezy. Some of these amebæ may normally inhabit the intestines of other animals; when it is considered how little is known of the intestinal protozoa of lower animals, and how extensively some of these protozoa can adapt themselves to " foreign " hosts, the reported occurrence of unfamiliar amebæ in human beings is much less common than might be expected.

Although species which show constant and distinctive morphological features ought, in the writer's opinion, to be regarded with an open mind, there is less to be said for the " physiological " species. Brumpt (1925) concluded that *E. histolytica* was really made up of two morphologically identical species, the true *histolytica* being large, of tropical distribution, violently pathogenic for cats, and a frequent cause of dysentery in man, the other, which he named *E. dispar*, being small, widely distributed in temperate as well as tropical climates, only mildly pathogenic for cats, and the cause of low-grade, chronic infections in man. Kessel's (1928) demonstration of the fact that identical diseases are caused in kittens by amebæ from acute amebic dysentery and by cysts from an apparently symptomless carrier, and by large and small cysts, adds weight to the doubts which practically all protozoölogists have with respect to *E. dispar*.

There has also been much discussion with respect to the identity of the human species of amebæ and morphologically identical ones found in other animals. Strict host specificity on the part of intestinal amebæ can no longer be accepted, although some protozoölogists have grimly adhered to belief in it in spite of growing evidence against it. The genus *Endamœba* is an excellent one to illustrate the situation. In man there are two universally recognized intestinal species, *E. coli* and *E. histolytica.* The latter species can be successfully transferred to such a variety of animals as monkeys, rats, guinea pigs, rabbits, cats, dogs and pigs. *E. coli* has been transferred to monkeys, cats and rats. In various species of lower primates, from spider monkeys (*Ateles*) to apes, indistinguishable forms of one or both of these types of amebæ have been described. Kessel (1928) showed that identical diseases were caused in cats by monkey and human *E. histolytica*, by either of these after being established in pigs, or by the *histolytica*-like amebæ naturally harbored by pigs. Five of the species of human amebæ (and 4 human flagellates) have been found by Kessel in Macacus monkeys, differing in no morphological or physiological respect from the corresponding protozoa in man. Natural infections with *E. histolytica* have been observed in most of the animals in which experimental infections have been produced. Kessel's (1923) successful experiments on the transfer of 5 different species of human intestinal amebæ to rats demonstrated that in spite of environmental changes the morphological characters of species and strains remain strikingly constant, whereas there is not

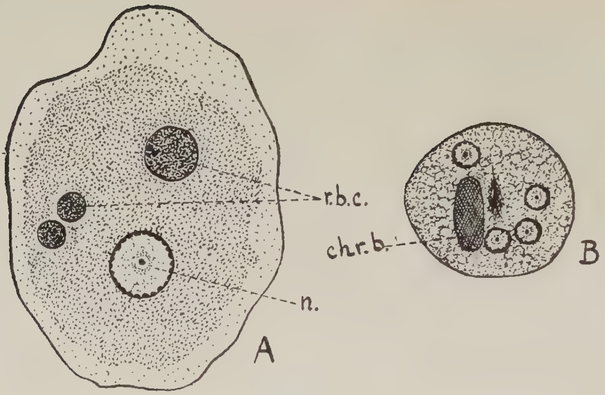

FIG. 16. *Endamœba histolytica.* × 1650. *A*, stained vegetative ameba; *B*, cyst with four nuclei; *n.*, nucleus, showing peripheral chromatin granules and central karyosome; *r. b. c.*, ingested red blood corpuscles; *chr. b.*, chromatoid body. (After Dobell.)

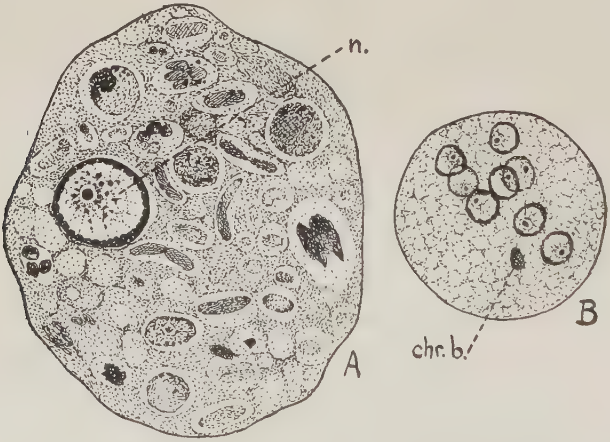

FIG. 17. *Endamœba coli.* × 1650. *A*, stained vegetative ameba; *B*, cyst, with eight nuclei; *n.*, nucleus, showing coarse peripheral chromatin granules, chromatin granules in "clear zone" between periphery and karyosome, and eccentric karyosome; *chr. b.*, remnant of chromatoid body. Note large number of food vacuoles in vegetative ameba. (After Dobell.)

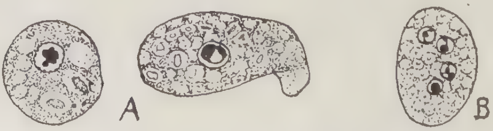

FIG. 18. *Endolimax nana.* × 1650. *A*, two stained vegetative forms, showing nuclei with large irregular karyosome, and numerous food vacuoles. *B*, cyst with four nuclei. (After Dobell.)

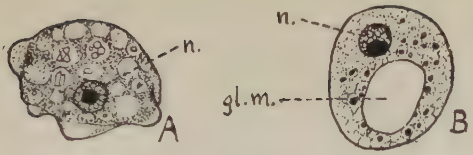

FIG. 19. *Iodamœba williamsi.* × 1650. *A*, stained vegetative ameba, showing numerous food vacuoles and nucleus (*n.*), the latter with large central karyosome and a single layer of granules between karyosome and nuclear membrane. *B*, cyst, showing nucleus (*n.*) with peripheral karyosome, and glycogen mass (*gl. m.*) or "iodophilic body," from which these cysts received the name "Iodine or I. cysts." (After Dobell.)

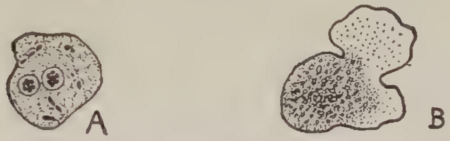

FIG. 20. *Dientamœba fragilis.* × 1650. *A*, stained vegetative ameba, showing two nuclei with granular karyosomes, and food vacuoles; *B*, living ameba, showing leaf-like pseudopodia. (*A*, after Dobell; *B*, after Jepps and Dobell.)

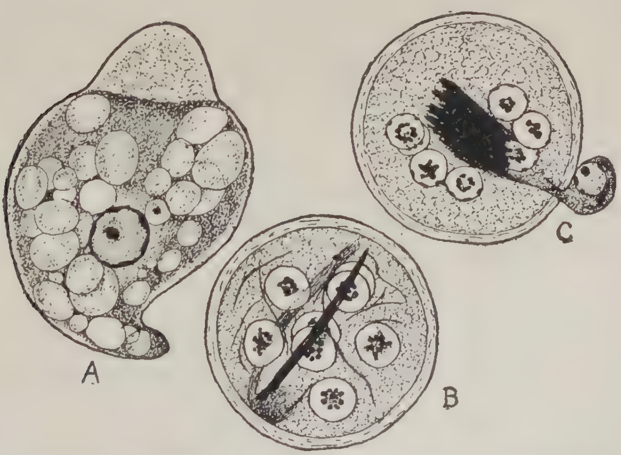

FIG. 21. *Councilmania lafleuri.* × 1650. *A*, stained vegetative ameba with a pseudopodium in early phase of protrusion and one nearly retracted and filled with endoplasm; nucleus showing peripheral chromatin and large irregular, eccentric karyosome; endoplasm filled with food vacuoles. *B*, cyst showing 8 nuclei, thick wall, and chromaphile ridge (dark) nearly encircling body, and chromatoid bodies in form of scattered threads. *C*, cyst showing bud escaping with one nucleus; large chromatoid body in center of cyst. (After Kofoid and Swezy.)

much to be said for a close limitation to specific hosts in a parasite which can infect such a variety of animals as primates, rodents, carnivores and pigs, when opportunity for infection is afforded.

The outstanding characteristics of the genera of amebæ which are generally recognized, and those which seem worthy of at least tentative acceptance, are as follows:

Endamœba; nucleus vesicular with chromatin arranged in a peripheral layer of bead-like granules of fairly uniform size, and a small compact karyosome; a capsule-like structure can usually be seen surrounding the karyosome. Cysts, if produced, with normally 4 or 8 nuclei of similar structure to those of the free forms, and including also glycogen masses and refractile "chromatoid" bodies, though these masses and bodies commonly disappear before or soon after the cysts become mature. (See Figs. 16 and 17.)

Endolimax; nucleus vesicular without a distinct peripheral layer of chromatin. A fairly large compact mass of chromatin (karyosome) in the interior, usually more or less eccentric and connected by threads or processes with one or more smaller masses. Mature cysts oval, with 4 nuclei in the known species, similar in structure to those of the free forms. The cysts contain, in addition to the nuclei, a number of small refractile granules of a substance known as volutin. The young cysts also contain masses of glycogen. (See Fig. 18.)

Iodamœba; nucleus vesicular with moderate-sized central karyosome and well developed membrane without a distinct peripheral zone of chromatin, but with a single layer of rather large granules between the karyosome and the outer membrane; cysts very characteristic, formerly known as Iodine cysts or I. cysts, of very irregular shape, containing, besides a single nucleus, a number of brightly refractile granules and a relatively large clearly defined solid mass of glycogen which stains very deeply in iodine. The nucleus is peculiar in that the karyosome comes to lie peripherally in contact with the nuclear membrane. (See Fig. 19.)

Dientamœba; mature individuals with two similar nuclei; these are vesicular with a large central karyosome consisting of a number of granules; nuclear membrane very delicate without distinct peripheral chromatin; cysts not found. (See Fig. 20.)

Councilmania; nucleus with a central karyosome composed of a number of small discrete granules; nuclear membrane faint, occasionally encrusted with chromatin but more often free from it, especially in cysts, or, in one species, with a heavy peripheral blob resting against the nuclear membrane on one side; cysts normally with 4 or 8 chromosomes, but occasionally more; buds containing single nuclei escape from a pore in the cyst wall until the cyst is emptied of all its nuclei; pseudopodia broad and clear, formed in a sudden explosive manner. (See Fig. 21.)

Karyamœbina; nucleus with chromatin massed in one or two, rarely more, crescentic clumps, semicircular in extent, on the nuclear membrane: large excentric round karyosome surrounded by a halo; in mitosis about 20 chromosomes form, with large polar caps of chromatin; pseudopodia clear; no cysts observed.

Endamœba histolytica

Unlike any of the other intestinal amebæ, this species does not feed on bacteria and other contents of the intestine of its host, but nourishes itself on the living cells and tissues. However, as James (1928) has pointed out, it is incredible, as is usually taught, that the majority of the motile amebæ (trophozoites) live *in* the tissues, for the number of amebæ found in dysenteric stools is out of all proportion to the number found in the tissues at autopsies, and there is often an enormous number of motile and encysted amebæ in stools during intervals between symptoms. Actual tissue invasion appears to be the part of the few rather than the many. It is possible, however, that the amebæ always nourish themselves at the expense of the host, but in the case of the majority they apply themselves to the surface of the mucous membrane and superficially dissolve the cells without burrowing in. It has been demonstrated that the earliest lesions of amebic infection are not ulcers, but superficial erosions. Ultimately ulcers form, and a certain number of the amebæ penetrate into the tissues, feeding on blood corpuscles and dissolved tissue juices.

E. histolytica, contrary to the older conception of it as a tropical parasite, has a world-wide distribution, and where routine examinations are made, even in England and various parts of the United States, 5 per cent to 10 per cent of the entire population is found to be infected. The figure is undoubtedly higher in the tropics, where obvious pathogenic conditions are of much more frequent occurrence. Knowles thinks that not less than 15 per cent of residents in the tropics are infected. In tropical America, at least, this figure is certainly too low; in some examinations in Colombia over 50 per cent of the population harbored this parasite, and the club servants, waiters and cooks revealed the astonishing and disconcerting incidence of 60 per cent. In Peking, China, Kessel and Svensson found 30 per cent of adult Chinese and 25 per cent of adult foreigners harboring this parasite.

In the motile stage *E. histolytica* is relatively large, and usually varies in diameter from about 20 to 30 μ, but larger forms occur and smaller ones, even down to an average of 10 to 12 μ, are sometimes found. About one-third of the ameba consists of clear, refractile ectoplasm, the rest being a finely granular endoplasm. In the fresh state, when warm, the amebæ are very active, and travel along in a straight line in a manner which Dobell describes as suggesting a slug moving at express speed; in this condition the rapidly advancing end of the body consists of a single clear pseudopodium, while ingested red corpuscles flow and roll about as though in a mobile liquid. Other amebæ have more tendency to stay in one place, where they extend and retract their pseudopodia without making much headway. The ingested red corpuscles, which usually number from 1 to 10, although there are sometimes over 40, are very characteristic, and in contrast to the miscellaneous food ingested by other amebæ. Sometimes when the stools are not bloody the amebæ may not contain them, but they do not contain bacteria or other débris, although rarely there may be tiny fragments of tissue cells. Any ameba found in a dysenteric stool and containing only blood corpuscles may safely be regarded, without further investigation, as *E. histolytica.*

After stools have been passed the amebæ begin to become abnormal and to die almost immediately, and they then present very different appearances, which has resulted in much confusion, for more often than not the stools are several hours old when an examination is made. The amebæ under these circumstances no longer travel, but remain in one place, throwing out large, dome-shaped, clear pseudopodia from different parts of the body; the endoplasm becomes full of vacuoles; and bacteria invade the dying body. The nucleus also disintegrates, and presents abnormal appearances both in fresh or stained preparations. Even in this condition the large amount of clear ectoplasm serves as a means of differentiation from *E. coli.*

The nucleus is so delicate in structure that it is practically invisible in fresh active forms. After being fixed and stained the nucleus has a characteristic structure. The nuclear membrane is encrusted with uniform fine granules of chromatin, and there is a small dot-like, central karyosome, surrounded by an indefinite, clear halo. Between the karyosome and the nuclear membrane is a clear area devoid of chromatin granules, marked by a linin network which often has a spoke-like radial arrangement. *E. coli*, on the other hand, has coarser and more irregular peripheral granules, a larger karyosome, excentric in position and with a more definite halo, and with usually a few chromatin granules strung on the linin network surrounding the halo; the nucleus of this species is visible as a bright refractile ring in fresh, living organisms.

E. histolytica multiplies by simple fission and a modified form of mitosis in which, according to Kofoid and Swezy, six chromosomes are formed (see Fig. 2, p. 32). Under certain conditions, instead of continuing active multiplication and growth, the amebæ become progressively smaller with relatively larger nuclei, probably as the result of division without corresponding growth; they round up and become inactive, and are then in the pre-cystic stage. It was formerly thought that encystment was a reaction to unfavorable conditions, — an attempt to protect against the exigencies of life in the outside world when leaving a host, but Boyers, Kofoid and Swezy have shown that encystment may occur in the tissues even when conditions of food supply and nourishment are favorable, and is to be interpreted as a naturally-recurring phenomenon in the life cycle, irrespective of environmental conditions. The sole purpose of encystment is, as Yorke and Adams say, the propagation of the parasite from one host to another. All contained food is either digested or thrown out, and a thin cyst wall is then formed. The nucleus is about one-third the diameter of the newly formed cyst. Most encysting individuals then lay down in the cytoplasm one or two massive, deep-staining structures which are called chromatoid bodies; in this species they are bar-like with rounded ends, quite different from the splinter-like chromatoid bodies of *E. coli*. In some individuals there is a distinct glycogen vacuole, but the glycogen is more often diffuse or absent, in contrast with early cyst stages of *E. coli*, which usually have well-marked glycogen vacuoles. The nucleus now divides into two and then four progressively smaller nuclei, thus forming a mature, four-nucleated cyst. These cysts are very characteristic, with their thin, round cyst walls, the four nuclei with the characteristic *histolytica* structure, the large chromatoid bars, and the absence of glycogen vacuoles. In fresh preparations they have a greenish tint and are refractile; if a preparation containing numerous cysts is viewed with a low-power objective slightly out of focus the cysts appear as little shining objects scattered through the preparation. Some writers have stated that rarely *E. histolytica* overshoots the mark and produces eight nuclei in the cyst, but most protozoölogists firmly deny this; Kofoid thinks the occasional 8-nucleated cysts attributed to this species may be cases of his *Councilmania dissimilis*. As the cysts grow older the chromatoid bars gradually disappear.

The size of the cysts varies from 5 μ to 20 μ in diameter, and there are a number of races or varieties of the ameba which differ from each other in the average size of cysts.

The cysts leave the body in various stages of development; seldom are more than 50 or 60 per cent mature when first passed, but it has been observed that such immature cysts can complete their development outside the body. The cysts, if kept moist and cool, and especially if placed in clean water, will live for a number of weeks. They are destroyed by desiccation and degenerate rapidly at high temperatures. If left in feces they do not survive more than from 3 or 4 to 10 days. Cysts, therefore, which reach water used for drinking or washing vegetables, or get into wet foods, are in an advantageous position both from the standpoint of length of life and of chances of causing infection. The criterion which has been extensively employed to determine the viability of cysts is the fact that dead cysts usually stain with eosin whereas living cysts do not, but this test is not infallible. The cysts have been shown to " hatch " in the same environment that they form, but there seems to be some substance present in feces which inhibits excystment. This, as Yorke and Adams point out, is a provision on the part of nature to keep the cysts from hatching in the host where they were formed, which would prevent them from fulfilling the purpose for which they were produced — the transfer to a new host. They do, however, hatch in the small intestine, and also in the large intestine, of cats. It is probable, therefore, that cysts passing down the bile ducts from the liver may cause repeated re-infection of the intestine.

It is only as cysts that the amebæ can survive outside the body, and apparently it is only in this form that the infection can be spread, for the motile forms seem unable to pass through the human stomach and small intestine and then cause infection in the large intestine. Hegner (1926), however, showed that one hour after motile *E. histolytica* from a culture were introduced into the stomach of a guinea pig, live moving specimens could be found from 6 to 51 inches behind the stomach, and Dobell and Laidlaw (1926) found that the motile amebæ could withstand 0.2 per cent hydrochloric acid for 30 minutes.

According to Yorke and Adams the amebæ escape from the cysts, in a suitable medium at body temperature, as four-nucleated bodies which subsequently divide, although the number of nuclei may multiply still more before division occurs. This is in contrast to the method of excystation which Kofoid and his colleagues have described in *Councilmania* (see p. 95).

E. histolytica was first successfully grown in culture by Boeck and Drbohlav (1925), and subsequently a simpler means of culture was devised by Craig (1926). The amebæ, if transferred to a fresh culture every day or two, can be kept going indefinitely. Strangely enough, they feed on bacteria in cultures, although they rarely if ever do so in the intestine; if blood corpuscles are present they devour these also. It has been suggested that the culture method may be successfully used for determination of percentage of carriers, rather than repeated microscopic examinations, or together with them.

Pathogenicity. — *Endamœba histolytica* is probably always at least mildly injurious to its host, but the old idea that acute dysentery is the typical effect produced by it is no longer tenable. The amebæ at first erode the superficial mucous membranes, either along the whole large intestine, or localizing in the cecum or other parts. Eventually eating into the tissues, the amebæ reach the submucosa and then extend their excavations laterally, beneath the surface, thus forming the typical flask-shaped ulcers. Fortunately the muscular coats of the intestinal wall usually act as a barrier, otherwise every amebic infection would soon cause perforation of the intestine with disastrous results for the patient. The ulcers vary greatly in number and size; in severe cases almost the entire colon is undermined. Ulceration of the bowel, however, is by no means always accompanied by dysentery or even diarrhea, though in the tropics this occurs in perhaps 10 per cent of cases; outside the tropics it is rare. The reason for this has been the subject of much speculation, and while some authors have supposed that less virulent strains of the parasite exist in temperate climates, others, notably Brug (1925), have found support for the idea that climate itself is in some way favorable to the production of dysenteric symptoms. Few workers believe in strains of varying virulence, and think the difference lies in the host rather than in the amebæ, but just how a tropical climate renders the host more susceptible has not been explained.

In amebic dysentery the stools, usually acid, consist of almost pure blood and mucus, in which swarms of amebæ, laden with blood corpuscles, are present. Such stools may be passed every few minutes, accompanied by intense griping pains. This condition may last for a few days or even a month, and may recur at intervals of months or years. More frequently, even when extensive ulceration is present, there is no dysentery but only vague abdominal discomfort and gastro-intestinal symptoms such as constipation, flatulence, passage of blood supposed to be due to invisible hemorrhoids, together with a feeling of fatigue, neurasthenia, etc. James estimates that in northern South America at least 25 per cent of obscure gastro-intestinal ailments, not manifested by dysentery or diarrhea, are due to amebic infection.

It is clear that the amebæ, actively dissolving the tissues, may frequently be drawn into the portal circulation. Such amebæ are carried to the liver, and usually settle there, continuing their attacks on the tissues. According to Knowles and others, probably the majority of individuals who harbor amebic infections in the colon are subject to repeated infections of the liver. Sometimes no obvious symptoms result, but in many cases there is a low grade of liver injury, and not infrequently one or several liver abscesses form. These are sterile so far as bacteria are concerned, unless secondarily infected; they may become very large and are filled with a slimy, bloody, chocolate-colored material resembling pus, but made up of dead amebæ, remnants of destroyed tissue, bile, etc., with active amebæ in the enlarging walls. Contrary to earlier opinion, Boyers, Kofoid and Swezy have shown that the amebæ encyst in the liver as well as in the intestine, and that the cysts pass out through the bile ducts to the small intestine.

Amebæ which have escaped into the blood stream are not necessarily halted in the liver, but may be carried to any part of the body. Lung abscesses are fairly frequent, either from rupture of a liver abscess into the adjacent lung or from amebæ carried directly by the blood stream. Next in frequence are abscesses of the brain. In 215 autopsy cases in Panama, extending over 22 years, these were the only two places where amebic infections beyond the liver were found. Other workers, however, have recorded amebic abscess of spleen, urinary bladder, genital glands, and skin, and Boyers, Kofoid, *et al.* have found *E. histolytica* in the bone marrow in a certain type of arthritis and in the lymph glands in Hodgkin's disease, as well as in skin ulcers. Such invasions appear, however, to be relatively rare, though theoretically they could easily occur. Boyers, Kofoid, *et al.*, however, believe that general systemic distribution of the amebæ commonly takes place, and a variety of symptoms, — gastro-intestinal, hepatic, nervous, pulmonary, etc., — almost as varied as in syphilis, and as hard to eradicate, may occur. However this may be, chronic conditions with indefinite symptoms are now known to be the rule in *E. histolytica* infections, and it is doubtful if really healthy uninjured carriers ever occur. Often, as in malaria, syphilis, and other protean diseases, a sort of truce is struck between the parasite and the host, with a relapse when the resistance is temporarily lowered by over-exhaustion, colds, or other unfavorable circumstances.

Diagnosis in acute cases of dysentery is easy, for the blood and mucus stools are swarming with active amebæ containing blood corpuscles. In chronic cases, on the other hand, repeated examination on successive days is required, with better chances of success if bile salts or magnesium sulphate is given. Examination of stained smears is more reliable than search in fresh stools. The presence of whetstone-shaped "Charcot-Leyden" crystals is strongly indicative, if not definitely diagnostic, of *E. histolytica* infection. As great danger lies in making a false positive diagnosis as a false negative one, for to inexperienced workers an ameba is an ameba, and often even epithelial cells and other objects are amebæ; many a patient, unfortunate enough to have an undiscriminating technician find an innocent *Endamœba coli* or *Endolimax nana* in his stools, has had to submit to a course of emetin which was useless if not injurious to himself, and quite innocuous to the amebæ. No doubt many patients with bacillary dysentery, having the numerous leucocytic cells diagnosed as amebæ, have been sent to the grave or had their illness intensified by a toxic course of emetin which was entirely uncalled for. Dobell in 1917 wrote: "The errors committed by an examiner with little or no previous experience are such as I could not have believed possible if I had not actually encountered them; and in cases where the health of a patient is at stake, it is, I believe, almost better that no examination at all should be made, than that it should be made by an incompetent and inexperienced person."

Other animals than man also suffer from amebic dysentery. In kittens experimental infections are very severe and usually fatal, and take a different course than in man; if recovery does occur the infection dies out instead of becoming chronic. A peculiarity of the infection in cats is the failure of the amebæ to produce cysts. Dogs can not only be experimentally infected but not infrequently become infected naturally. In India, and probably in other parts of the tropics, dogs very commonly devour human feces and must often consume enormous numbers of amebic cysts. Whether these all "hatch," or are destroyed, or are passed through uninjured, is so far unknown. The possibility exists that dogs, and perhaps also pigs, which harbor amebæ indistinguishable from *E. histolytica* as well as many other intestinal protozoa morphologically like those in man, may play an important rôle in the dissemination of the disease. No one has yet discovered cysts in the feces of infected dogs; if, as in cats, none are formed, the dangerousness of dogs would be much less. Rats also can be experimentally infected, and spontaneous infections of rats have been reported, though some protozoölogists question these observations because of the difficulty of distinguishing the natural amebic infections of rats. Rats commonly inhabit sewers, and must frequently feed on substances contaminated by cyst-laden feces; there is, therefore, little reason to doubt that rats may play some part in the disemmination of human amebæ.

Treatment and Prevention. — Like many other protozoan diseases, amebiasis, if left untreated, tends to become chronic and to persist indefinitely. As in other protozoan infections, also, there are a number of more or less "specific" drugs which, when administered to acute cases, almost immediately bring about brilliant, almost magical, results. The unfortunate part of it is that the results are seldom permanent, and it has even been questioned whether a complete cure of amebic infection could ever be attained. When the nature of the lesions produced by amebæ is considered, one wonders at the optimism of a physician who gives a few doses of a drug and then turns his patient loose without further thought as to diet or after-treatment; ulcers of stomach or duodenum are not so lightly treated. Although the stools of patients usually become entirely free from either motile or encysted amebæ within a few days after treatment with the specific drugs, they tend to reappear, sometimes soon, sometimes after long intervals, unless the treatment is continued for a long time. Even then relapses are common; it is possible that the amebæ bring the process of elimination to a halt by encysting, but how long they may persist in the body as cysts it is impossible to say; they may instead flourish locally as motile forms in pockets in the tissue of liver or intestinal wall, where the drugs do not reach them in sufficient concentration to kill, but where the development of local immunity usually prevents them from making great headway, and they may subsequently escape again to the lumen of the intestine, where the whole process is repeated. This would seem to be the more probable by analogy with similar relapses in other protozoan infections. Malaria parasites, leishmanias, trypanosomes, etc., do not encyst in the human body, but limited numbers of them do for a long time escape the action of drugs which kill the majority.

The first discovered and still the most widely used " specific " drug for treatment of amebic infection is emetin, an alkaloid prepared from ipecac, which is extracted from the roots of a Brazilian herb. Emetin hydrochloride injections bring about results in acute cases which are amazing both in their extent and rapidity, but in chronic cases they are less effective; many workers prefer another preparation, emetin-bismuth-iodide, which is given by mouth. More recently two other drugs have come into prominence, stovarsol, an arsenic compound, and yatren, an organic compound of iodine. Yatren can be given by mouth, by enema, or by injections, is not toxic to the host, and gives remarkably good results, even in cases where the other drugs fail. Combination treatment with emetin and one of the other drugs is believed by many to give the best results.

The essentials in the prevention of amebic infection are sanitation and cleanliness. Infection results only from the swallowing of cysts passed in the feces. It is obvious that the cysts may gain access to the mouth in two principal ways, — (1) by contamination of food or water from feces not sanitarily disposed of, and (2) by soiled hands, resulting in a finger-to-mouth infection, direct or indirect. By the former method cysts from stools deposited on the ground, as is almost universally the custom in the tropics, are washed into water of wells, tanks, or streams used for drinking or washing vegetables; or, being scattered by rain or surface washing, or by the use of night-soil for fertilizer, they adhere to such fruits and vegetables as lettuce, radishes, strawberries, etc.; or they may be deposited on food by flies or roaches which have ingested them or have picked them up on their filthy feet. It is obvious that prevention of infection by this route consists in a sanitary disposal of feces, protection of water supplies from pollution, and either avoidance of uncooked vegetables or their sterilization. It is customary for Europeans in India to soak uncooked vegetables in a potassium permanganate solution for an hour, but usually several cooks have to be discharged before one is finally found who will actually carry out what he considers a silly notion, rather than risk being caught not doing it. Even then he feels that if he sets a head of lettuce in an inch of "red water" he has sufficiently carried out instructions. Immersion for 30 seconds in water at 80° C. has also been recommended. The excellent results which may come from protection of water supplies from pollution are demonstrated by Clark's (1924) figures in Panama, where a good water system was installed in 1914–15. Between 1905 and 1914, 4.25 per cent of 4000 autopsies showed amebiasis, while from 1914 to 1923 there were only 0.28 per cent among 2800 autopsies.

The finger-to-mouth method of infection is thought by some to be even more important than the contamination from feces. The infection tends to spread in families, and some workers think that the main source of contagion lies in the contacts which the infected person makes with utensils, wash bowls, towels, or other objects which the soiled hands may contaminate, or more especially with food in markets, restaurants or homes. James recommends that Europeans in the tropics should insist on all servants cleaning their hands thoroughly with scrubbing brush, antiseptic soap and water several times a day, especially before preparing or serving food. This is excellent advice, but in India, at least, one would have to stand over each servant with both eyes wide open during the entire process of each washing, and very likely have to render assistance!

In addition to the fecal contamination and soiled-hands methods of infection, the possibility of spread by animals, especially dogs and rats, must not be forgotten. Rats may directly transmit infection by contamination of food with their droppings; dogs by licking the hands or faces or dishes with soiled tongues; and pigs or other animals by adding to the sources of fecal contamination.

Other Intestinal Amebæ

The other amebæ which inhabit the human intestine would be of very little consequence if it were not for the danger of confusion between them and *Endamœba histolytica*. They are never tissue parasites, and there is no good evidence that a human being is any worse off for harboring these guests in his intestine. They all ordinarily live free in the lumen of the intestine, at least so far as is known at present, and fail to show the fastidiousness with respect to food that *E. histolytica* shows; instead they feed on bacteria, small cysts, starch grains, and all sorts of débris found in the semi-fluid medium in which they live. In other respects, such as life cycle, mode of encystment, resistance in the cyst stage, mode of transmission, transferability to other kinds of animals, etc., they appear to be all very similar to *E. histolytica.*

Endamœba coli. This is the commonest of the human intestinal amebæ, and has been stated to occur probably in 50 per cent of human beings; its distribution is world-wide; according to Dobell " no race, nor any country, has yet been discovered in which infections with this species are not common." The motile forms are found especially in the upper part of the large intestine, and the precystic and cyst forms lower down.

Although undoubtedly this species is to be regarded as a harmless commensal, there is some evidence that it may rarely invade tissues. Contrary to earlier opinion it may occasionally include red blood corpuscles in its diet, and Brumpt found specimens in small ulcerations in the intestine of a kitten artificially infected with both this species and *E. dispar* (his supposedly non-pathogenic strain of *E. histolytica*). It is quite likely that *E. coli* did not itself cause the ulcers but merely wandered into them, for there is no evidence that it has a tissue-dissolving ferment; the occasional ingestion of blood corpuscles is to be expected on the part of an animal which displays as little selection in its diet as this one does.

The outstanding characteristics of *E. coli* (Fig. 17) have been mentioned in connection with its differentiation from *E. histolytica*, but they may advantageously be summarized again. The living forms are usually 20 to 30 μ in diameter, and never as small as the smallest races of *histolytica.* The body usually has very little ectoplasm, and even the ponderous pseudopodia are usually composed mainly of endoplasm, although clear ones are occasionally produced. Unlike *histolytica* this ameba tends to move about sluggishly in one place without making much headway in any one direction. The body is usually crammed with food vacuoles, for it is a voracious feeder. Knowles says he has several times seen this ameba with an ingested starch grain almost as large as itself, apparently half-paralyzed with lethargy after such an enormous meal. The nucleus is clearly visible in living specimens as a refractile ring.

In stained specimens the contained food and the nucleus distinguish it from *histolytica.* The nucleus has a coarser peripheral layer of chromatin, a larger and excentrically placed karyosome, and usually dots of chromatin strung on the linin network.

Encystment occurs precisely as in *E. histolytica*, except that eight instead of four nuclei are produced. The precyst stages are the most difficult to distinguish from those of *histolytica;* it can only be done by the nuclear structure in good specimens.

The cysts have thicker walls than those of *histolytica;* in the 2-nucleated stage there is usually a very large glycogen vacuole which nearly fills the cyst, lying between the nuclei, but it begins to become diffuse even by the time the cyst becomes 4-nucleated. The mature cysts, which are most commonly found in fresh stools, are from 15 to 22 μ in diameter, have 8 nuclei of the typical *coli* type, more granular cytoplasm than in *histolytica*, and either no chromatoid bodies or else a few flakes like splintered glass, never the heavy bars found in *histolytica.* According to Hegner, the cysts hatch as entire 8-nucleated amebæ.

Councilmania. Kofoid and Swezy (1921) observed some amebæ which they believed had previously been confused with *E. coli*, but which they think are quite distinct, and should belong to a separate genus. This species, which they named *Councilmania lafleuri* (Fig. 21), is very active and creeps about with remarkable activity. It commonly produces only a single pseudopodium at a time, and this is composed entirely of clear ectoplasm; it is peculiar in being shot out almost instantaneously for the greater part of its length. The endoplasm is usually loaded with food vacuoles containing bacteria, etc., and also frequently blood corpuscles, from which circumstance it is thought that it may be mildly pathogenic. The nuclei differ from those of *Endamœba coli* in having very little peripheral chromatin and in having the karyosome in the form of several approximated but distinct granules without a halo. There are said to be eight chromosomes as in *E. histolytica*, and not six as in *E. coli.* A peculiarity on which Kofoid and Swezy laid considerable stress is the method of escape of amebulæ from the cysts by a repeated process of budding, a single nucleus at a time slipping out through a pore in the cyst wall, surrounded by a part of the protoplasm (Fig. 21C). Two species of rat amebæ were also assigned to this genus. In 1927 Kofoid described another new *Councilmania*, *C. dissimilis*, which he believes in the past has been confused with larger races of *E. histolytica.* The outstanding feature is the nucleus, which in both motile and encysted stages has a large lateral blob of chromatin, with little peripheral chromatin elsewhere, and a central karyosome of dispersed granules; it is said to form 8 chromosomes. Budding is said to occur as in *E. lafleuri.* The cysts (Fig. 22*B*) contain 4, or rarely 8, nuclei. In 1928

Kofoid added the species *tenuis*, originally described by Kuenen and Swellengrebel as an *Endamœba*, to the genus *Councilmania*. Its cysts (Fig. 22*A*) are commonly ellipsoidal or asymmetrical, and the nuclei have very little or no peripheral chromatin and a karyosome formed of an aggregate of several granules. The motile amebæ are only 7 to 10 μ in diameter, while the cysts, which have 4 or rarely 8 nuclei, have an average mean diameter of about 7 μ. Budding occurs less frequently than in the other species. *C. dissimilis* was encountered in 0.4 per cent of 2587 examined persons, and *C. tenuis* in 9.2 per cent.

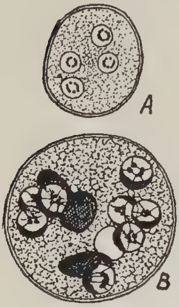

FIG. 22. Cysts of *Councilmania tenuis* (*A*), and *C. dissimilis* (*B*). × about 1500. (After Kofoid.)

These species of amebæ have not been generally accepted by other protozoölogists, and particular exception has been taken to the budding process, which others construe as being merely rupture of cysts under tension. However this may be, the morphological characters, especially of the nucleus, which the writer has himself seen in slides supplied by Kofoid, are distinctive. The fact that these species retain their characteristic features in carriers up to four years (in the case of *C. lafleuri*), in cultures, and even after transfer to rats, and are not merely occasional forms found here and there and not followed up, make some of the criticisms of their validity, and suggestions that they are abnormal, injured, or badly prepared representatives of other species, seem rather prejudiced.

Another common intestinal ameba of man is *Endolimax nana*, (Fig. 18), the principal characteristics of which are given under the genus *Endolimax* on p. 84. It is a small ameba measuring from 6 μ to 12 μ in diameter. It creeps sluggishly like *E. coli*, and, like that species, often contains numerous food vacuoles filled with bacteria. The four-nucleated cysts (Fig. 18*B*) might be confused with those of *E. histolytica*, but are distinguishable by their small size (usually 8 to 10 μ by 7 to 8 μ), their oval shape, and the peculiar structure of the nuclei, described on p. 84. This is a very common human parasite, having been found in as high as 33 per cent of some series of examinations made by competent workers. Although frequently found in dysenteric patients associated with *Endamœba histolytica*, there is no evidence that this species is at all pathogenic. Like *E. coli*, this ameba cannot be eliminated by emetin or any other drugs although it temporarily disappears during emetin treatment. Its exact habitat in the intestine is not known, but it is certainly not a tissue parasite. *Endolimax nana* also occurs in monkeys and probably identical forms occur in rats and pigs; a form differing only in its smaller size has also been described from a guinea pig. Other probably different species occur in frogs, lizards and fowls.

Iodamœba williamsi (Fig. 19) is a small ameba (usually 9 μ to 13 μ in length) the nuclear characteristics of which have been sufficiently described on p. 84. The motile ameba has no clear differentiation between ectoplasm and endoplasm, and is usually sluggish in its movements, like *Endolimax;* Smith (1928), however, found freshly excysted individuals to be surprisingly active. They feed promiscuously on minute particles, such as bacteria. The cysts of this species (Fig. 19*B*) were formerly thought to be of vegetable nature and were known as Iodine or I. cysts. The cysts are not smaller than the free amebæ; they are of very irregular shape, as if formed under pressure. When placed in a fluid medium at body temperature the cysts hatch in a few hours. They also do this in guinea pigs and rats, but while the rats become infected, the hatched amebæ die very soon in the cecum of guinea pigs. Monkeys also harbor this ameba, and pigs are so commonly infected that this animal is believed to be the normal host. Cauchemez estimates that 50 per cent or more of pigs in France are infected, and Feibel found 20 per cent of pigs slaughtered in Hamburg harboring it. It is found all over the world and has been estimated by Hegner and Taliaferro to infect 10 to 15 per cent of human beings. This is another example of the close parasitological relations between pigs and man.

Another very small human ameba, *Dientamœba fragilis* (Fig. 20), has been described by Jepps and Dobell. This species averages only about 8 or 9 μ in diameter, thus resembling *Endolimax nana.* The free amebæ are active, showing well marked ectoplasm and endoplasm. The pseudopodia are of ectoplasm, and are flat and leaflike (Fig. 20*B*). The peculiar features of the organism are described on p. 84. The most characteristic feature of this ameba is the division of the nucleus shortly after cell division has occurred, so that mature individuals have two similar nuclei. Cysts of this species have not been found either in infections or in culture except in one case by Kofoid, and some protozoölogists think that what he interpreted as cysts were really only rounded-up forms of the motile amebæ. It is probable either that cysts are formed, since the amebæ are very short-lived outside the body, or else that the ameba is normally a parasite of another animal and fails to produce cysts in man because of its abnormal environment, as is the case with *Endamœba histolytica* in cats. The habits of this ameba are apparently similar to those of other non-pathogenic forms. It is a rare human parasite; Taliaferro and Becker in 1924 had records of only 33 cases, and a few have been found since; it has, however, a wide geographical distribution.

Karyamœbina falcata is a species which Kofoid and Swezy have described from six cases in 3000 examined. No cysts have been found. It has clearly-separated ectoplasm and endoplasm, and a heavy peripheral pellicle. The nucleus contains one, two, or more crescentic chromatin masses applied to the nuclear membrane, and a spherical excentric karyosome in a halo. The mitosis resembles that of the free-living ameba, *Vahlkampfia,* in the formation of heavy polar caps and a large number, about 20, chromosomes, but differs from *Vahlkampfia* in that the polar caps are not formed by the karyosome. This ameba, like *Councilmania,* has been rejected by Wenyon as probably an *Endamœba.* But, as Kofoid points out, an ameba with twenty chromosomes cannot possibly be identical with one having only six. Very likely this species is not normally a human parasite, but more likely a parasite of some other animal, which is able occasionally to establish itself in man.

Mouth Amebæ

In contrast to all other amebæ living in man, or even in animals, there is one species of *Endamœba, E. gingivalis*, which inhabits the mouth instead of the large intestine. Goodrich and Mosely (1916) have found what seems to be the same species in pyorrheal pus from the mouths of dogs and cats; Nieschulz (1924) found a similar form in accumulations around the teeth of horses; and Kofoid (1929) found all the monkeys he examined infected with an apparently identical ameba, the more heavily infected ones showing conditions closely resembling human pyorrhea. Dogs with inflamed gums or pus pockets were infected with human mouth amebæ. In man it can be found in a high percentage of individuals, increasing with advancing age until, according to Kofoid, 75 per cent or more of people over 40 harbor it. It has a marked resemblance to *E. histolytica*, but Kofoid and Swezy have called attention to distinct differences. It is about 12 to 20 μ in diameter, and has even more crystal-clear ectoplasm than has *E. histolytica* (Fig. 23). The vacuolated endoplasm is usually crowded with food particles which seem to float in the center of large, fluid cavities. The pseudopodia are normally broad and rounded, like large blisters, and the ameba progresses rapidly in various directions, though its pseudopodia and movements may be quite altered by exposure to shocks, such as an altered medium or temperature. The nucleus has the peripheral chromatin in more uneven granules, and the karyosome consists of several closely associated granules. Whereas the *E. histolytica* nucleus has a clear halo around the karyosome and a finely granular outer zone between the halo and the nuclear membrane, *E. gingivalis* has a granular cloudy halo, especially dense around the karyosome, and a clear outer zone, through which a few spoke-like strands of linin run (Fig. 23*C*).

Unlike its close relatives this species fails to form cysts; apparently the ease and rapidity with which infections can spread from one human mouth to another does away with the biological necessity for cysts. As would be expected of an organism inhabiting the mouth, it is rather more adaptive to changing environmental conditions than are the intestinal amebæ. It will survive for 20 minutes at a temperature of 45° C., and shows remarkable resistance to low temperatures. Miss Koch (1927) showed that some amebæ were still alive after 48 hours at 15° C., and some will survive for 18 hours at the freezing point. They survive the shock of exposure to a wide range of hydrogen ion concentration, and are not at all fastidious as to the chemical constituents of a culture medium. They survive on a slide for three minutes after all visible moisture has disappeared, the minute amount of water retained by tiny particles of coagulated egg from the culture being enough to keep them alive.

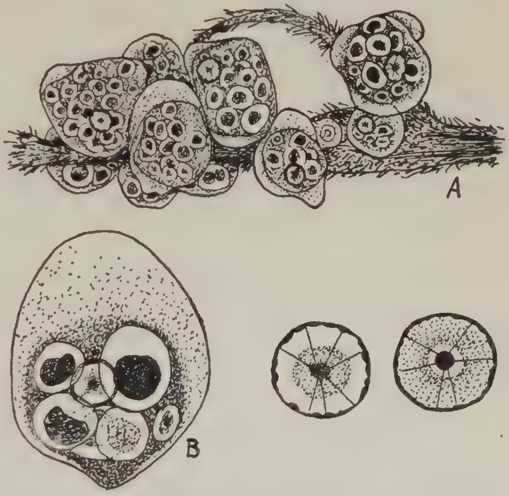

FIG. 23. *Endamœba gingivalis.* *A*, cluster of amebæ on filamentous mass of *Leptothrix*, containing large numbers of food vacuoles with remnants of nuclei of leucocytes; *B*, an ameba in locomotion with characteristic single broad pseudopodium. *C*, Comparison of nuclei of *E. gingivalis* (left) and *E. histolytica* (right). (After Kofoid and Swezy.)

The food habits of *E. gingivalis* have been the subject of much dispute. The food vacuoles sometimes contain bacteria, but they most often contain what are unquestionably the nuclei of lecuocytes, in various stages of digestion (Fig. 23). Goodey and Wellings (1917) concluded that these were "salivary corpuscles," *i.e.*, nuclei of disintegrating leucocytes, which are abundant in saliva, but Child (1926) found undoubted evidence of the ingestion of whole leucocytes as well as remnants of dead ones, and in cultures Miss Howitt (1926) found that they ingested both red blood corpuscles and leucocytes obtained from the peritoneum of guinea pigs. She also made the interesting observation that red blood cells lying on a slide in the vicinity of an ameba faded from view within five minutes while those in the surrounding medium remained intact. If the amebæ can not only digest blood corpuscles inside their bodies but also secrete an enzyme which will dissolve them before they are taken inside the body, it is possible that they might also dissolve other tissue cells as does *E. histolytica.* It might even be possible that in the case of leucocytes they might dissolve the cytoplasm outside the body and then ingest and rapidly digest the nuclei for which they seem to have an inordinate fondness. Sometimes partly liquefied viscous nuclear material is spit out from an individual food vacuole and is taken up by a neighboring ameba, so that the two are temporarily attached by a strand of this partly digested material.

Pathogenicity. Although the presence of amebæ in the mouth has been known for many years, no one took much interest in them until Bass and Johns (1914) and Barrett (1915) demonstrated an apparent relation between these mouth inhabitants and the presence of pus pockets between the teeth and gums, a disease known as pyorrhea, from which a high percentage of human beings suffer. These little pockets erode the delicate peridental membrane surrounding the roots of the teeth (Fig. 24), which corresponds in a general way to the periosteum of the bones. The erosion of the living membranes of teeth and gums is accompanied by a constant formation of pus and a proneness of the gums to bleed, often without provocation. Absorption of waste products causes more or less noticeable constitutional symptoms, such as disordered digestion, nervous troubles, rheumatic pains, etc. As the ulceration of the membrane continues, the tooth is gradually loosened from the gum. Just as meadow mice girdle fruit trees, so pyorrheal infections eat away the living "bark" of the teeth, eventually causing them to fall out. Over 50 per cent of all permanent teeth which are lost fall out as the result of pyorrhea.

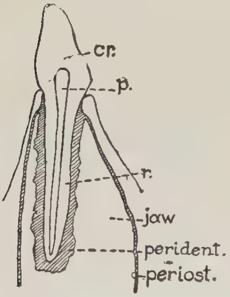

FIG. 24. Sketch of tooth showing peridental membrane, which is the tissue attacked by *Endamœba gingivalis* and the seat of pyorrhea; *perident.*, peridental membrane; *periost.*, periosteum; *cr.*, crown; *r.*, root; *p.* pulp. (After Bass and Johns.)

Whether the formation of pus pockets is initiated by the amebæ or by other organisms is not known, but certain it is that *Endamœba gingivalis* is nearly always, perhaps always, present in the lesions, and at the very bottom of them, often buried in the inflamed tissues to a depth of several times its own diameter. However, after this ameba had had the spotlight turned on it for two or three years on account of its apparent association with pyorrhea, it fell into obscurity again with almost as dramatic suddenness because a number of workers, including Craig, Dobell, and others, vigorously denied its claim to prominence. Their arguments were based principally on the frequent occurrence of the ameba in apparently normal mouths, its occasional absence in cases of pyorrhea, and particularly the failure of emetin, which acts so powerfully against *E. histolytica*, to bring about improvement in the disease, and the assertion that the ameba feeds only on dead and disintegrating tissues. Recently interest in this little parasite has been revived by Kofoid and his students. It has been conclusively shown that it is a species quite distinct from *E. histolytica*, and therefore the frequent failure of emetin to improve the disease has little weight as evidence against its hand in the proceedings; emetin seems to be specific against *E. histolytica* alone, and Miss Howitt has shown that it is tolerated to a remarkable degree by *E. gingivalis* in culture. From a recent survey of 350 individuals by Hinshaw (1926), using the cultural method of diagnosis, which is more accurate than microscopic examination, it was concluded that protozoan parasites do not occur in normal mouths, whereas *E. gingivalis* occurs in most, if not all, cases of incipient to advanced pyorrhea. The further demonstration that this ameba ingests both red corpuscles and leucocytes, and perhaps even excretes a tissue-dissolving enzyme, leaves the burden of proof with those who believe in its innocence. The amebæ are often very localized in the mouth, and are only present in the pus pockets. They do not tolerate association with putrefactive bacteria of decaying débris, and so cannot be regarded as scavengers. Apparently they cluster about on the strands of filamentous bacteria which are involved in the formation of tartar, and prey upon the nuclei of the swarming leucocytes, without invading the adjacent gum tissue (Fig. 23*A*). The bony tissue between the teeth and below the level of the tartar is extensively eroded without accompanying evidence of infection by either bacteria or amebæ. The host reacts to the stimulus of this combination of bacteria, amebæ and tartar by an active and continuous accumulation of leucocytes and resulting flow of pus. Even if it should be demonstrated that the amebæ do not actually initiate the ulcerations, but merely find a pleasant field of activity in them after bacteria have started them, one must be very generous to absolve them from complicity in their extension. The amebæ exhibit a peculiar adhesive quality and frequently drag along behind them large clumps of bacteria; such transportation of bacteria to the depths of the pus pockets may in itself be injurious, even if the amebæ do not directly attack other tissues than the leucocytes.

Pyorrhea is not the only pathological condition with which *E. gingivalis* is associated. The parasite was found by Smith, Middleton and

Barrett to be a common invader of the crypts of infected tonsils, where, as in the mouth, it may be presumed to do some mechanical injury if it does not actually attack the living tissues. The same authors suggested a possible relation, through injury to the tonsils, to certain types of goiter. The possibility has been suggested that *E. gingivalis* might occasionally make its way through the digestive tract and be confused with *E. histolytica* in the feces, but Miss Howitt found that its susceptibility to free acid would rarely allow it to pass the stomach, and even if it did so, it would probably be destroyed by bile in the small intestine, which causes it to shrink up rapidly and then explode like a bombshell. The chances of finding *E. gingivalis* in the feces, therefore, seem very slight.

Treatment and Prevention. Ordinary cleanliness of the mouth, by frequent brushing of teeth, rinsing of the mouth, and care of imperfect teeth, is the most important factor in protecting the gums against the formation of pus pockets, but such methods are of little or no avail after the disease has started. There is no good remedy known for amebic infections of the mouth. Earlier work indicated that emetin in the form of mouth washes or injections had a beneficial effect not only in eliminating amebæ, but also in improving pyorrhea, but subsequent work has shown that the action of emetin is very unreliable, and that *E. gingivalis* is much less susceptible to it than is *E. histolytica.* Miss Koch (1926), however, has shown that certain dyes, especially acriflavine, are destructive to the amebæ in culture in high dilution, and that in these dilutions they are not injurious to the gum tissue of normal rabbits; she suggests the possibility of their use as mouth antiseptics.

While it is still uncertain to what extent, if at all, amebæ are involved in causing or aggravating pyrorrhea, it would seem to be the course of wisdom to avoid them as far as possible. They are undoubtedly spread not only directly from mouth to mouth, as in kissing, but also by minute droplets expelled in coughing or sneezing, and by means of drinking glasses, spoons, etc., on which it is evident that they can live as long as a trace of moisture remains. It is probably impossible, however, to avoid occasional infection with *E. gingivalis.* One cannot always make a protozoölogical examination of a mouth before indulging in a kiss, nor can one be sure that a cook has not coughed during the preparation of a meal! If, however, the mouth is kept scrupulously clean and in as near perfect condition as possible, the amebæ may be less likely to find a congenial place to settle down; in most mouths, on the other hand, there is plenty of hospitality offered to them.

CHAPTER VI

INTESTINAL FLAGELLATES AND CILIATES

Flagellates in General

The flagellates (Class Mastigophora) surpass all other protozoa in numbers of individuals, and in variety of environments successfully occupied. Free-living forms range from the " red snows " of the polar regions and Alpine summits to the ooze of the ocean's depths. They swarm in seas, lakes, rivers, puddles and soil; they abound in decaying organic matter, and in feces and sewage, and play a part in the transformations attendent upon putrefaction and decay; they inhabit the bodies of the majority of species of animals and many plants, and invade most organs and tissues, even to the innermost recesses of the human brain. They may nourish themselves like plants by utilizing sunlight and chlorophyll, like animals by actively devouring living or dead organisms, like bacteria or fungi by absorbing dissolved organic matters, or as parasites by preying on living animals which harbor them. They afford valuable material for the study of many fundamental biological problems.

The classification of this great group of primitive organisms is still in an uncertain state. Most protozoölogists divide them into two subclasses: Phytomastigina, including plant-like forms, and Zoömastigina, including animal-like forms, but the division is more or less arbitrary. All the parasites of mammals belong to the Zoömastigina. So much difference of opinion exists concerning their further subdivision into orders and families that a discussion of this is best omitted here. For practical purposes we can divide the parasitic flagellates of vertebrates into (1) the intestinal flagellates, including with them the few forms found in the mouth and vagina, and (2) the hæmoflagellates which live in the blood and tissues of their vertebrate hosts, and often in one phase of their life cycle in the gut of insects. For the sake of completeness we may mention that there is another quite distinct group of complex flagellates, parasitic in white ants, which possess many nuclei and blepharoplasts and numerous flagella.

The human intestine furnishes a habitat for a considerable number of protozoa in addition to the amebæ discussed in the previous chapter, but is not so subject to such inhabitants as are the digestive tracts of many lower animals, especially the ruminants. As in the case of the amebæ, the majority of flagellates which live in the digestive tract are believed to be of little pathogenic importance, though opinions differ on this point. There is only a single species of ciliate which habitually inhabits the human intestine, but this one, like *Endamœba histolytica*, is frequently a true tissue invader and a cause of severe dysentery. There are also several coccidians which are intestinal parasites of man, but these will be discussed in a separate chapter dealing with the Sporozoa.

Intestinal Flagellates

The human " intestinal " flagellates which are commonly recognized belong to five genera, of which *Trichomonas* lives in the mouth, large intestine and vagina; *Chilomastix*, and probably the rarer *Embadomonas* and *Enteromonas*, live in the large intestine; and *Giardia* lives in the small intestine.

In some respects nearly all the flagellates which make their home in the digestive tracts of animals resemble one another. Nearly all of them, with the conspicuous exception of *Trichomonas*, secrete for themselves resistant transparent cysts which protect them from drying up or from the presence of an unfavorable medium. The unencysted protozoans which may be carried out of the intestine die quickly and probably could not produce a new infection even if swallowed immediately, since in some species, at least, they are unable to withstand the action of the acid juices of the stomach. None of the human intestinal flagellates requires a second host to transmit it as do the blood-dwelling parasites. While outside the body they remain dormant in their cysts for weeks or months until they can gain access to a host again through food or water. There is still much doubt as to the extent to which intestinal protozoans are confined to particular hosts. Some workers believe that each animal has its own species peculiar to it, and that these species do not normally infect other hosts. Evidence is accumulating, however, to show that in some cases, at least, this is not so, and that many intestinal protozoans of man are able to live in such animals as rats, mice and hogs. Most intestinal protozoans are of very wide geographic distribution, their abundance in any given place being largely determined by the warmth of the climate and the sanitary, or rather unsanitary, conditions.

Naturally these parasites are seldom discovered except when there is some intestinal ailment, since in normal health feces are seldom submitted for examination. Where routine examinations have been made regardless of physical condition, it has been found that a large per cent of people in unsanitary places are infected. Stiles, in a town in one of our southern states, found that from 50 to 100 per cent of the children were infected, and it would probably be easily within the bounds of truth to say that 75 per cent of all people in warm countries, living in places where unsanitary conditions prevail, are subject to infection with one or several species of intestinal protozoa. As Stiles has pointed out, such infection usually means that the infected person has swallowed human excrement, since it would be impossible for any natural agency to separate the microscopic protozoan cysts from the feces in which they are found. This fact, impressed upon the mothers of infected children, especially when accompanied by the remark that one could not tell whether the infection had come from the excrement of a white or a negro, was found by Stiles to be one of the most powerful means of improving sanitary conditions in the South.

In the following paragraphs the several genera of human intestinal flagellates are discussed with reference to their structure and identification, and what is known of their life cycles, habits and pathogenic effects.

Trichomonas

Trichomonas is one of the commonest flagellates found in the human intestine. It makes its home in the upper part of the large intestine and cecum, sometimes multiplying in prodigious numbers, but it is often difficult to find in the feces except in diarrheic conditions. A *Trichomonas* also lives in the vagina and in the urinary tract, being quite often found in vaginal discharges, especially in cases of leucorrhea. Hegner found it in 50 per cent of women examined in Honduras, and other authors elsewhere give estimates between 10 per cent and 20 per cent. It is still questionable whether this parasite is a separate species from the intestinal forms, but it is usually distinguished by the name *T. vaginalis*. Hegner has succeeded in establishing an intestinal *Trichomonas* of a monkey in the vagina of a monkey. There is also a *Trichomonas* found in the mouth of man and dogs, which is known as *T. buccalis* (or *elongata*); it more closely resembles the vaginal form than it does the intestinal ones, but shows some structural and cultural peculiarities. Until recently it was regarded as a rather uncommon parasite, but Hinshaw, using cultural methods, found it in 40 per cent of people whom he examined who were over 30 years of age! A trichomonad which is probably the same as this is sometimes found in bronchial and pulmonary infections. It is still a debated question whether the trichomonads of vagina, intestine and mouth are entitled to be considered separate species. The difficulties, however, do not end here. *T. vaginalis* and *T. buccalis* (or *elongata*), as well as the intestinal form which is commonest in temperate climates, *T. hominis*, all have four anterior flagella, but other intestinal forms have been found which have three, and others five. These breed true to type, and there is no evidence yet adduced that these flagellates can or do change the number of their flagella under any conditions. There is, furthermore, evidence that the five-flagellated form is fairly strictly limited to a tropical distribution, sometimes to the exclusion of the others, and is much more commonly associated with a persistent type of diarrhea for which most workers consider it responsible. Recent work by Cleveland on the three-flagellated form, on the other hand, shows that it is coprozoic and can live even on hay infusions, and is possibly representative of the opposite extreme as regards pathogenicity. In view of these facts, it seems justifiable to regard these different types of intestinal trichomonads as at least separate species, if not genera. The five-flagellated form (Fig. 25*A*) has been named *Pentatrichomonas ardin-delteili*, and the coprozoic three-flagellated one *Tritrichomonas fecalis*. Trichomonads also live in a vast variety of other animals including mammals, birds, reptiles, amphibians, fish and even invertebrates. Some of them have structural characteristics peculiar to them, and therefore deserve recognition as separate species, but the various species are extensively transferable from one type of host to another (*e.g.*, *Tritrichomonas fecalis* from man to frogs, many mammalian Trichomonas to chicks, etc.). Such facts are very annoying to those protozoölogists who believe in a fairly strict host specificity of intestinal protozoa!

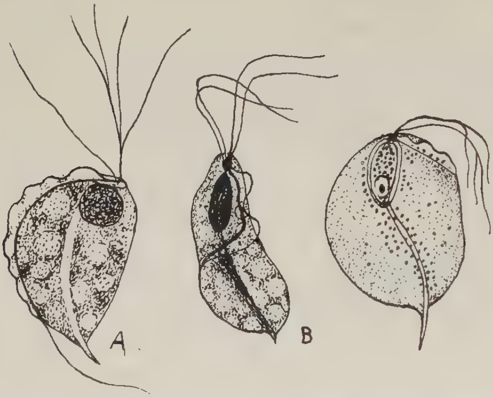

Fig. 25. *A*, *Pentatrichomonas ardin-delteili*, after Kofoid and Swezy; *B*, *Trichomonas buccalis*, after Goodey and Wellings; *C*, *Trichomonas vaginalis*, after Hegner. × about 1400.

The trichomonads (Figs. 25 and 26) are more or less rounded or pear-shaped organisms which are easily recognized either when alive or after staining by their characteristic structure. They vary in size from only 5 or 6 μ in length up to about 25 μ, but they are most frequently between 10 and 20 μ in length with a width about two-thirds as great. There are, as already noted, either three, four or five long, slender anterior flagella, but in all cases one of these, which is longer than the others, is independent, while the rest are in a cluster and move by simultaneous strokes. Along one side of the body there is an undulating membrane to the margin of which is attached another flagellum, the end of which may or may not extend free beyond the end of the membrane. The undulating membrane may be less than half the length of the body, as is usually the case with *T. vaginalis*, or it may extend almost to the posterior end and be continued as a free flagellum half the length of the body, as in *Pentatrichomonas.* The body is supported by a stiffened rod, the axostyle, which frequently projects free at the posterior end, like a little tail spine, being especially long in *Tritrichomonas.* The unexposed part of this is hard to see in living flagellates; in stained specimens it may be clear, or studded with deep-staining granules, according to the species; in *T. vaginalis* the granules are in rows beside the slender axostyle, and also scattered in the cytoplasm (Fig. 25*C*). The nucleus is round or oval, in the anterior part of the body, and varies in its appearance when stained according to the stage of its activity. Sometimes it has few or many scattered granules of chromatin, while at other times it seems to have a single large central granule. The flagella arise from blepharoplasts, but there is a difference of opinion as to the number and arrangement of these; it seems clear that the independent flagellum and undulating membrane are connected with a separate blepharoplast from the other flagella, as would be expected if, as is believed, the blepharoplasts are the centers of a sort of nervous control over the movements. Along the base of the undulating membrane there is a deep-staining basal rod. In some forms there is a fairly prominent cytostome or cell mouth on the side of the nucleus opposite the undulating membrane, but in *T. vaginalis* and *T. buccalis* this is very indistinct and apparently vestigial. It is significant that these forms usually have very little evidence of ingested food as compared with the intestinal forms, which often have numerous food vacuoles.

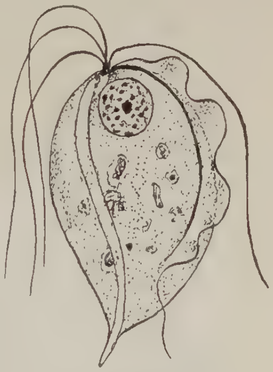

FIG. 26. *Trichomonas hominis.* × 3000.

Trichomonas is a very agile little animal, and swims with a characteristic wobbly motion, by synchronous beats of its clustered flagella and independent beats of the independent one, along with synchronous undulations of the membrane. The fore part of the body is very flexible, but the hind part is fairly rigid. It feeds in part on bacteria and in part, probably, by absorption of dissolved substances, and probably all species ingest red blood corpuscles when they are available. It multiplies by simple fission, but when multiplication is rapid the growth of the body and multiplication of the nuclei outstrips the division of the cytoplasm so that large multinucleate bodies are formed. There is no evidence that any of the species encyst, and this process seems not to be a biological necessity, for the motile forms live in undiminished numbers for several hours, and some individuals for days, in the feces. They are very hardy for intestinal parasites, and will withstand temperatures up to 44° C. for two hours, and live for a long time at very low temperatures.

Although long regarded as a harmless animal, it is becoming increasingly evident that some, at least, of the trichomonads are not as innocuous as they were thought to be. *Pentatrichomonas*, particularly, is very commonly associated with a persistent type of diarrhea with fetid, yellow-brown stools. Knowles (1928) says, "one must admit that, clinically, the more one sees of infection of man with *T. hominis* (*Pentatrichomonas*), in Calcutta, the more one comes to associate it with a chronic and very intractable diarrhea," though he further remarks that a clinical impression is very likely to be wrong, and that the subject requires further study. Kessel (1928) found kittens in China naturally infected with a form morphologically like the four-flagellated *T. hominis;* all had diarrhea, two had dysentery, and all died inside a week. Other kittens were infected from these and died of the same symptoms in 12 days, and still others, infected with *Trichomonas* from man, monkey and rat, developed the same symptoms. When examined at autopsy there was catarrhal inflammation in the intestine, necrosis of the superficial layers of the mucous membrane, and sometimes superficial ulcers, with Trichomonas in the necrotic lesions, between the cells, and in the enlarged glands. Trichomonads do invade the body, for they have been found in blood smears, and in pus from amebic abscess of the liver, and Wenyon has found them in the tissue of the intestinal mucosa. *T. vaginalis* is commonly associated with diseased conditions of the vagina, but there is no positive evidence that it causes the trouble. *T. buccalis* has always been regarded as harmless, but Hinshaw has found it definitely associated with advanced, inflammatory pyorrhea. Thus there is, in this disease, in addition to filamentous bacteria, amebæ, and various other organisms, this flagellate to be taken into consideration. A disease, as Kofoid (1929) ably makes clear, can no longer be regarded as dependent on the simple presence of one causative organism; it must rather be considered as the product of the interaction of many factors, of which the host and parasite each play leading rôles, but in which there may be many other secondary but contributing factors. The biologist who tries to assign to each factor its share in the process has a herculean if not impossible task. In the present instance, neither the amebæ nor the flagellates, which are so constantly present in advanced cases of pyorrhea, can be lightly disregarded as having no influence on the course of events.

In comparison with the other human trichomonads, *Tritrichomonas fecalis* is very versatile, and while it is evidently able to survive as an intestinal parasite of man, it seems to do better as a free-living form. It increases enormously in diluted feces and in all sorts of outside environments, and Cleveland found it quite contented to live in the intestines of frogs and tadpoles, though he showed that it was not identical with *Tritrichomonas augusta* so commonly found naturally in those animals. It is very improbable that this form can have any pathogenic significance.

Chilomastix mesnili

It is a remarkable fact, which beautifully exemplifies how recent is any accurate knowledge of human intestinal protozoa, that this organism, in spite of its very clearly marked characteristics and the fact that it can be found in from 3 to 10 per cent of human beings, was not recognized as a distinct species until 1910. Like most of the other intestinal flagellates it has had a long list of "aliases."

In many respects it shows relationship to *Trichomonas*, and is often found associated with it, and by careless observers is often confused with it, though it has strikingly different morphological features. Like *Trichomonas* it is an inhabitant of the large intestine, and closely similar forms are found in all groups of vertebrates. They are common in both rats and frogs.

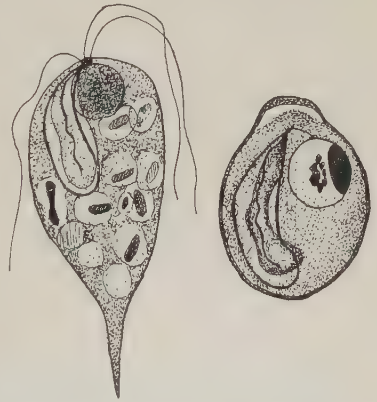

FIG. 27. *Chilomastix mesnili*. Left, active form; right, cyst. × 3000. (After Boeck.)

Chilomastix (Fig. 27) is an unsymmetrical, pear-shaped animal which has its posterior end drawn out into a sharply-pointed tail. It varies in length from 6 to 20 μ, but the usual length is from 10 to 15 μ. The body is less plastic than in *Trichomonas*, so there is less variability in shape. It has three slender anterior flagella which, like those of *Trichomonas*, function as two groups, two of them lashing back against the left side of the body, and one against the right. There is a relatively enormous cytostome or cell mouth, which is an oval groove half or more the length of the body, the lips of which are supported by a complicated system of fibers. Lying in this groove is a fourth flagellum, attached to the left lip by an undulating membrane; by its flickering movements this " tongue " wafts food particles into the depths of the groove, where they pass into the body to be enclosed in food vacuoles, with which the body is often literally crammed. The nucleus lies in the fore part of the body, just behind the free flagella.

The animals do not move as rapidly as *Trichomonas*, and proceed by a sort of jerky spiral movement, unlike the continuous wobbly progression of *Trichomonas.*

The ordinary multiplication is by simple fission, but sometimes, as in *Trichomonas*, the cytoplasm is unable to keep up with the pace set by the nucleus, and large multinucleate forms are produced. Unlike *Trichomonas, Chilomastix* forms lemon-shaped cysts, with the anterior end narrower. The cysts are usually about 7 to 9 μ long; they have thin walls, and the fibers of the cytostome, practically unaltered in form, lie alongside of or overlapping the nucleus. Occasionally the nuclei and cytostomal fibers are duplicated in the cysts, which then presumably give rise to two individuals when they hatch. The cysts are very resistant and live for months in water at room temperature, and for several days in the intestine of flies. Boeck found that a temperature of 72° C. was necessary to kill them.

There is less suspicion attached to *Chilomastix* with respect to pathogenicity than in the case of either *Trichomonas* or *Giardia.* It has never been observed to ingest blood corpuscles, and there is no evidence yet of ability to invade tissues.

Giardia

Giardia, which for many years was known as *Lamblia,* still suffers from disagreement as to what its species name should be, but *Giardia lamblia* seems to be the proper designation. It is one of the commonest inhabitants of the human intestine, especially in children, and probably affects at least 15 per cent of all human beings. Unlike any of the other intestinal flagellates, it makes its home in the small, not the large, intestine, especially in the duodenum. It is a very persistent parasite, and infections often last for years. Giardias also occur extensively in various kinds of mammals and birds, and also in amphibians. Most of those found in warm-blooded animals have only minute, and for the most part average, differences, and their specific distinctness is still open to question.

Giardia is a most fantastic little animal in appearance. It belongs to a group of flagellates which are spoken of as Diplozoa, or double animals, due to the fact that in its adult state it is perfectly bilaterally symmetrical, with nucleus and all other parts reduplicated on the right and left sides. It can be conceived of as analogous to two *Chilomastix*-like flagellates fused together in the middle line. As Knowles remarks, the student's first sight of a dead *Giardia*, in its motile phase, is apt to give him a shock, for it is as if a wizened monkey face were looking up at him from the other end of the microscope tube. The outline of the body is strikingly like that of a tennis racket without the handle. In side view it is seen that it is shaped like a pear split in two parts, lengthwise, with the flat surface in the broadest part gouged out as a large concave sucking disc, with slightly raised margins. The finely-tapering tail end is usually turned up over the convex back. There are eight flagella, one pair attached at the tip of the tail, the others emerging from the body at various points as shown in Fig. 28. They may be thought of as corresponding more or less to eyebrows, moustaches and beard. The body is from 10 to 18 μ in length. The two nuclei have large central karyosomes. Between them, running longitudinally through the body, are two slender rods, the axostyles, to which the nuclei are anchored, so to speak, by slender fibrils. There is a complicated system of basal granules and fibrils connecting with the flagella and the rods supporting

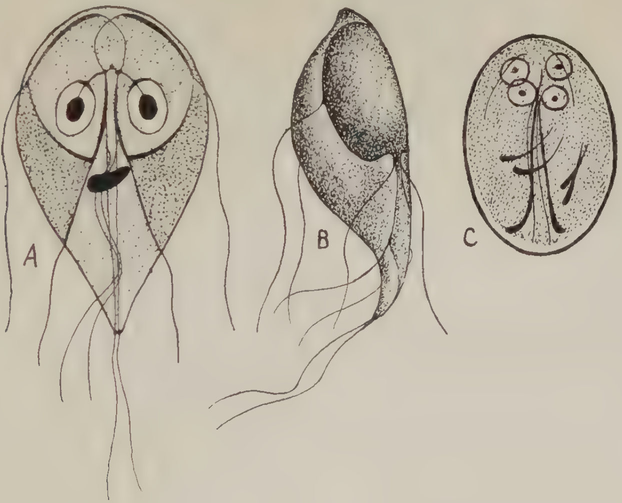

FIG. 28. *Giardia lamblia.* *A*, face view of active flagellate; *B*, semi-profile view; *C*, cyst. × 3000. (*A*, after Simon; *B* and *C*, original.)

the sucking disc, which can best be seen from Fig. 28. There are also one or two deep-staining, rather variable comma-shaped bodies lying just behind the disc, which have been interpreted as parabasal bodies. In life these grotesque little creatures fasten themselves by their hollow faces to the convex surfaces of epithelial cells in the small intestine, their flagella streaming like the barbels of a catfish (Fig. 29). Sometimes large areas of epithelium are practically covered with them, each one perched on a separate cell. Their vast numbers can be judged from the fact that in one instance Miss Porter estimated the number of cysts in a single stool to exceed 14,000,000,000. The number of cysts in an average stool in a case of moderate infection she estimated at over 300,000,000. The motile forms are not normally found in the stools, but in cases of diarrhea dead ones may be present in considerable numbers.

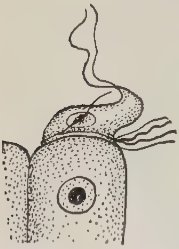
FIG. 29. *Giardia lamblia* resting on epithelial cell. × 1000. (After Grassi and Schewiakoff.)

Multiplication occurs by division into two in a plane parallel with the broad surfaces, and occasionally multiple fission occurs as in other intestinal flagellates. The cysts are formed intermittently; enormous numbers may be found on one day and then none for several days, when a shower of them again appears. During encystment a thick wall is secreted, and the cyst assumes an oval form, measuring 8 to 14 μ in length, commonly about 10 μ; usually the contents shrink away a little from the posterior end, leaving an empty space. At first the cyst contains a sort of "shadow outline" of the motile animal, with the two large nuclei anteriorly, the axostyle rods lying more or less diagonally, and a pair of curved deep-staining bodies which are variously interpreted as the parabasals or the detached supporting fibers of the disc. Division now takes place in the cyst, first of the nuclei and then of the fibrils, and there may be even further multiplication. Usually the four nuclei, now spherical, are clustered at one end, but they sometimes come to lie in pairs at opposite poles. According to Hegner (1927) the division of the flagellates is not completed until after the cyst hatches, which it does within 30 minutes after ingestion by a host, or when exposed in saline to a temperature of about 39° C.

The pathogenicity of *Giardia* is a much-debated question. The infection, especially in children, is commonly associated with an intractable, recurring diarrhea with large quantities of yellowish mucus in the stools, in which myriads of *Giardia* cysts, and often many dead motile forms, are present. It seems reasonable to suppose that the irritation set up by the parasites attached to the epithelial cells is sufficient to bring about an excessive secretion of mucus, and derangement of the normal digestive process. *Giardia* does not ingest solid food, nor does it appear to dissolve the tissue cells; possibly it feeds on the mucous secretions. It is, of course, not reasonable to suppose that the diarrhea is caused by the flagellates merely because of their presence in the liquid stools, but the frequent absence of other evident causes, and the high frequency of diarrheas in which *Giardia* is present, is at least cause for suspicion. Westphal and Georgi (1923) have also found *Giardia* in the gall bladder under conditions of chronic digestive disorders accompanied by jaundice, and they think that the flagellates may cause inflammatory conditions of the gall bladder and bile duct.

Other Intestinal Flagellates

There are a few other flagellates which sometimes live as residents of the human intestine, but they are relatively rare and of little importance. One of these is a little slipper-shaped animal, *Embadomonas intestinalis*. It was first discovered by Wenyon and O'Connor (1917) in Egypt, but has subsequently been found in many parts of the world, though always rare. The fact that members of the same genus occur in various insects, especially aquatic ones, and in frogs and turtles, suggests that the infections of man and other mammals in which they have been found may perhaps be derived from swallowing of cysts of some insect or aquatic species with water. Its rarity makes it doubtful if it is normally a human parasite.

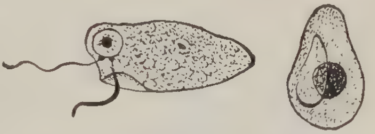

Fig. 30. *Embadomonas intestinalis*. Left, active form; right, cyst. × 3000. (After Wenyon and O'Connor.)

Embadomonas (Fig. 30) is very small, only 4 to 9 μ in length and 3 to 4 μ in breadth; it has two flagella, a long, slender anterior one, and a shorter, thicker one which lies partly in a large, elongated cytostome, the borders of which appear to have supporting fibers. The nucleus is anterior in position. The cysts are whitish, opalescent, pear-shaped bodies, 4.5 to 6 or 7 μ long when living. When stained they show what appears to be the karyosome of the nucleus, sometimes dumb-bell shaped, and fibers which Wenyon interprets as the marginal fibers of the cytostome.

Faust has described an *Embadomonas sinensis* from China which is larger and is said to have the two flagella alike, but Wenyon believes it is identical with *E. intestinalis*. As far as known, this flagellate lives in the large intestine and feeds on bacteria. It has been successfully cultivated.

Another rare human flagellate (Fig. 31) is a very small oval or rounded organism, 4 to 8 μ in length, with one trailing flagellum and a cluster of three anterior ones. Wenyon and O'Connor described this organism in 1917 and named it *Tricercomonas intestinalis*, but in 1915 da Fonseca described a similar one as *Enteromonas hominis*, but saw only two anterior flagella. If these two are identical the latter name is the right one to use, but opinion is divided on this point. Wenyon thinks some of the supposed cases of *Enteromonas hominis* were really small *Chilomastix*. Small oval cysts, 6 to 8 μ long, with from 1 to 4 nuclei, are formed. The 4-nucleated cysts have two nuclei at each end. These organisms are probably only accidental parasites of man, which are able to persist in the human intestine for only short periods.

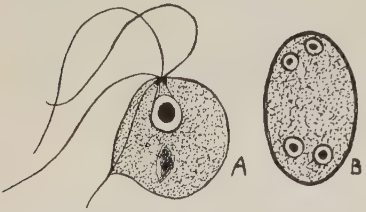

FIG. 31. *Tricercomonas intestinalis.* *A*, active form; *B*, cyst. × 3000. (After Wenyon and O'Connor.)

Still another rare human parasite which is clouded with uncertainty is *Craigia hominis*, originally described as an ameba with a flagellated stage. It was said by Craig to multiply during the amebic stage, to form cysts in which there are produced numerous "swarmers" which escape and develop a single flagellum each, then to multiply as flagellates for a time, finally losing the flagellum and resuming the ameboid state. Most writers think that known amebæ and flagellates have been confused. Kofoid and Swezy (1921) describe an undoubted round flagellate with a single delicate flagellum, which they assume to be *Craigia hominis*, but, as Wenyon (1926) indicates, there is little reason to connect it with the organism described as *Craigia*.

Coprozoic Flagellates

Other flagellates have from time to time been described as human intestinal parasites, but many of them are in reality coprozoic forms, the cysts of which have passed through the digestive tract uninjured. The coprozoic flagellates are commoner than coprozoic amebæ, and need a little consideration, since they have in the past, and no doubt will in the future, confuse many unsuspecting investigators. Two genera are especially common, *Cercomonas* and *Bodo;* both have one anterior and one trailing flagellum, the latter often more or less adherent to the body. *Bodo* has an indistinct cytostome and a large parabasal body, both of which are lacking in the less common *Cercomonas.* Many medical writers, untrained in protozoölogy, still refer to any and every flagellate found in the feces as "Cercomonas." They are small organisms, usually 5 to 10 μ long. *Bodo* often inhabits the large intestine of cold-blooded animals, but seems incapable of establishing itself in warm-blooded ones. Its cysts, which are 5 to 7 μ long, are oval and thin-walled, with usually a single nucleus, are widely distributed and find their way into distilled water, saline, etc., and turn up in blood smears, urine, etc., to the confoundment of unwary laboratory workers. As Dobell remarks, almost everyone who has studied these organisms has given them new names, so they have impressive lists of "aliases." Figure 32 shows the appearance of the motile and cyst stages of these confusing flagellates.

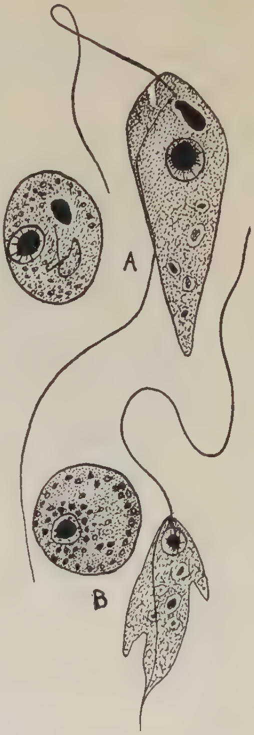

FIG. 32. Coprozoic flagellates. *A*, *Bodo caudatus*, active form and cyst; *B*, *Cercomonas crassicauda*, active form and cyst. × 3000. (After Dobell and O'Connor.)

Intestinal Ciliates

Although the digestive tracts of herbivorous animals commonly swarm with ciliates of many different kinds, only one species, *Balantidium coli*, is a common human parasite, although several other kinds, of doubtful status, have from time to time been described.

Balantidium coli (Fig. 33), as found in man, is much larger than any of the other protozoan inhabitants of the human intestine, and measures, usually, from 50 to 80 μ in length, with a breadth between $\frac{2}{3}$ and $\frac{3}{4}$ as great. In pigs it sometimes reaches a length of 200 μ. It is shaped like an egg or pear, and has at the anterior end an obliquely arranged depression, the peristome, which may appear wide open or slit-like, and in the bottom of which is the cytostome. The whole body is covered with fine cilia arranged in rows, with a special row of longer "adoral" cilia surrounding the peristome. The nucleus is sausage-shaped and usually lies obliquely near the middle of the body, with the small micro-nucleus often in a depression against it. There are two contractile vacuoles, and food vacuoles circulate in the endoplasm. Like other ciliates, *Balantidium* divides by transverse fission, a new cytostome being formed by the posterior daughter. Conjugation of two individuals enclosed in a cyst has been described by Brumpt. Ordinarily the thick-walled cysts, however, contain a single individual, which at first is still provided with slowly moving cilia. Later all characteristic structures except the nucleus disappear, but refractile bodies, which are probably in the nature of reserve food material, can often be seen (Fig. 33*B*). There is no evidence of multiplication in the cysts, which are probably purely protective.

Balantidium coli is a common inhabitant of the intestines of monkeys and pigs as well as of man, and pigs are usually regarded as the normal hosts; at any rate they are undoubtedly important reservoirs. McDonald (1922) believes that the pig harbors two species, only one of which occurs in man. A smaller species, *B. minutum*, was described from man by Schaudinn in 1899, but no unquestionable records of it have been found since. Other species occur in many animals, and they are almost always present in frogs and other amphibians. Cockroaches also harbor one or more species.

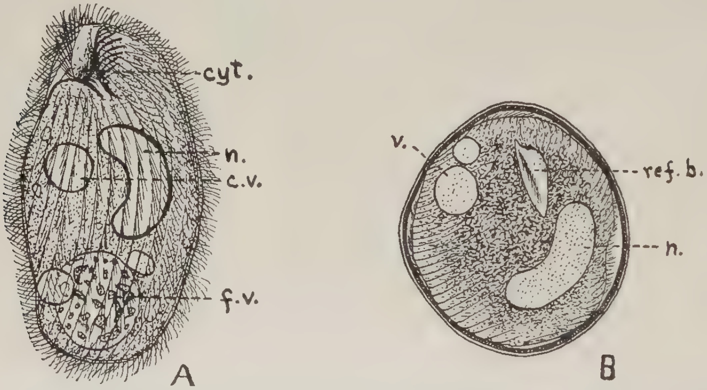

FIG. 33. *Balantidium coli.* *A*, active form from intestine; *c. v.*, anterior contractile vacuole; *cyt.*, cytostome; *f. v.*, food vacuole; *n*, nucleus. *B*, living cyst as seen in feces of pig; *ref. b.*, refractile body; *v.*, vacuole. × about 500. (*A*, after Wenyon; *B*, after Dobell and O'Connor.)

There is no question but that *B. coli* is a pathogenic parasite, closely resembling *Endamœba histolytica* in its activities. It causes ulceration of the large intestine, invades the tissues, and frequently, though not in the majority of cases, causes diarrhea or a severe and often fatal dysentery. Sometimes, at post-mortem, the large intestine is found in a horrible condition, ulcerated from end to end, with shreds of mutilated or dead tissue hanging from the walls. Many infected individuals who show extensive bowel ulceration, however, do not develop dysentery, a condition strikingly like that existing in the case of the dysentery ameba. There is no good evidence that this ciliate can establish itself in other parts of the body as does *E. histolytica*, though there are rare records of its occurrence in the bladder, lung and blood.

The only other ciliate recorded as a human parasite is *Nyctotherus faba*, found by Schaudinn in the same case as *Balantidium minutum*. It is a flat kidney-shaped ciliate with a cytostome situated in the notch in the middle of the body. There have been a few subsequent discoveries of this or supposedly related organisms about which little is known. Cockroaches commonly harbor a species of *Nyctotherus*.

As in the case of amebæ and flagellates, coprozoic ciliates are common, and have misled more than one parasitologist.

Treatment and Control of Intestinal Flagellates and Ciliates

Up to the present time no specific drugs for the cure of flagellate or ciliate infections have been found. Nearly every drug reputed to have any action against any protozoan or worm parasite has been experimented with, and many have been thought to be efficient, only to be discarded later. Many false hopes have been inspired by the fact that most of these organisms are intermittent in their appearance, and often spontaneously cease to be in evidence for considerable periods of time. No doubt, however, some, perhaps most, of the drugs which have been especially recommended do reduce or even cure a percentage of cases; none, however, seem to be wholly reliable.

Another method of approach towards control of at least some flagellates has been suggested by the work of Hegner and his students on the effect of diet on flagellates in rats and other animals. Hegner found that a diet rich in carbohydrates favored an abundance of *Trichomonas*, whereas a protein diet inhibited them. Ratcliffe (1928) concluded that the number of *Trichomonas* was inversely proportional to the abundance of proteolytic anaerobic bacteria, which are favored by a protein diet. A casein diet is especially effective in promoting the growth of these bacteria in rats and thereby reducing trichomonads. The acidity of the large intestine, though somewhat influenced by the diet, appeared to have little to do with the alterations in flora and fauna. Reis (1923) observed a similar association of *Balantidium* infections with acid-forming rather than alkali-forming bacteria. A survey of known infections of animals demonstrates the rarity of flagellate and ciliate infections in carnivorous animals as compared with their abundance in herbivorous ones, such as ungulates, rodents and primates. A few cases of treatment of human " flagellate diarrhea " with a carnivorous diet have been recorded and were successful. *Giardia* cases respond less quickly than *Trichomonas*, as would be expected in view of its situation in the small intestine, where bacterial changes are less easily induced, but they nevertheless appear to respond. It is doubtful whether protozoa like *Endamœba histolytica* and *Balantidium coli* would be affected at all after they have invaded the tissues, but those in the lumen probably would be. It is possible that the greater frequency of flagellate diarrheas and of protozoan dysenteries in the tropics may be due in part to the diet high in carbohydrates and low in proteins found in many tropical countries.

Since infection depends on the ingestion of cysts or, in the case of *Trichomonas*, motile forms passed in the feces of infected man or animals, avoidance of infection depends on precisely the same factors as in the case of amebæ, — sanitary disposal of feces, protection of food and water from contamination, and cleanliness on the part of infected individuals who can and do spread the infections by means of soiled hands. Since, as with the amebæ, such animals as pigs, rats and dogs can become infected with human flagellates and ciliates, the rôle of these animals in the spread of the infections must not be lost sight of.

CHAPTER VII

HÆMOFLAGELLATES — I. LEISHMANIA AND HERPETOMONADS

The Trypanosomidæ

The term "hæmoflagellates" is used for those flagellates which habitually live in the blood or tissues of man or other animals. There are only two kinds of these which occur in man, namely the Leishman bodies, belonging to the genus *Leishmania*, and the trypanosomes, belonging to the genus *Trypanosoma*. These two types of organisms, however, are only two of a number of genera which all belong to one family, Trypanosomidæ. Other members of the family occur as gut parasites of insects, and still others as parasites of plants. Since both the hæmoflagellates and the plant parasites undergo cycles of development in the gut of insects, which serve as intermediate hosts and vectors, and since a wide variety of insects, many of which are not blood suckers, have Trypanosomidæ in their intestinal tracts, it is safe to presume that this group of flagellates, among which are numbered some of the most deadly of human parasites, were originally and primitively parasites of the guts of insects, whence, by a process of adaptation to blood or plant juices in the intestines of the insects, and subsequent inoculation into the bodies of the plants or animals on which the insects habitually feed, they have transferred their sphere of activity, in at least part of the life cycle, to the hosts of the insects.

Four distinct morphological types of these parasites are found in the bodies of insects, as follows:

(1) The *Herpetomonas* type. (Fig. 34*C*.) This is the most primitive type, in which the body is more or less elongate or pear-shaped; it contains a nucleus near the center, a parabasal body near the anterior end, and a single long slender flagellum which arises from a basal granule closely associated with the parabasal body. All the other types of Trypanosomidæ may be considered as having arisen from this.

(2) The *Crithidia* type. (Fig. 34*B*.) This differs in that the flagellum arises from a kinetoplast (basal granule and parabasal body) which has shifted back to a position just in front of the nucleus, and is connected with the body, up to the anterior end, by an undulating membrane.

(3) The *Trypanosoma* type. (Fig. 34*A*.) In this the kinetoplast has moved far behind the nucleus to a point near the posterior end of the

body, and the flagellum is attached to the body, for almost its entire length, by an undulating membrane.

(4) The *Leishmania* type. (Fig. 34*D*.) This is a rounded-up form which contains a nucleus and a kinetoplast, but is entirely devoid of a flagellum. Any of the other three types may assume this form, and conversely may be developed out of it.

Any or all of these forms may occur in the digestive tracts of insects, but only the leishmania and trypanosome forms occur in the blood of vertebrates.

The fact that some flagellates never develop farther than the herpetomonas form, and others never, so far as known at present, farther than the crithidia form, while the trypanosomes go through all the stages, makes a study of this group of flagellates very confusing. When a herpetomonas or crithidia type is found in an insect gut it is impossible to say, without further investigation, whether it is an adult animal which never undergoes any further development, or is only a developmental phase of a trypanosome of a vertebrate animal. In recent years a number of crithidias which were supposed to be purely insect parasites, with no trypanosome stage, have been found to develop into trypanosomes in the blood of certain vertebrates, so it may be that most of the crithidias are really developmental stages of these parasites.

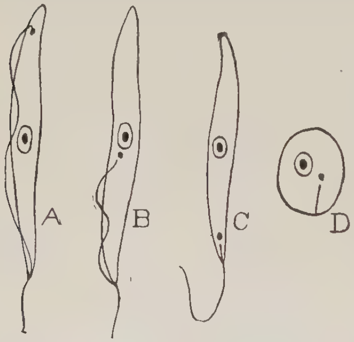

Fig. 34. Diagram of forms assumed by Trypanosomidæ, either as adults or as developmental forms; *A*, *Trypanosoma;* *B*, *Crithidia;* *C*, *Herpetomonas;* *D*, *Leishmania.* (After Wenyon.)

The Trypanosomidæ are usually divided into four genera on the basis of the life cycle, though some protozoölogists recognize more; these are *Herpetomonas*, *Leishmania*, *Crithidia*, and *Trypanosoma*. *Herpetomonas* includes those species which exist only in the leishmania and herpetomonas form, and occur only in insects and a few other invertebrates, and as parasites in various plants, especially Euphorbias and milk-weeds. They occur very commonly in various kinds of bugs, and in the larvæ and adults of fleas, many kinds of flies, mosquitoes, and other insects. The forms in fleas are of particular interest because of the confusion which they caused in the course of experiments directed towards proving that the Mediterranean form of kala-azar, and leishmaniasis of dogs, was transmitted by fleas. The herpetomonads of insects live almost exclusively *behind* the stomach, attached to the epithelial cells by their flagellar ends, the free flagella being very short or lacking; often they occur in rosettes of dozens of individuals (Fig. 35). In the posterior end of the intestine they become shorter and assume the leishmania form, and appear to develop a cyst wall, for they have been shown by Wenyon to resist drying for 24 hours. The larvæ of fleas, which habitually feed on blood defecated by the adults, become infected by these leishmania forms. Noguchi (1926) has shown that different strains of insect and plant flagellates differ amongst themselves, and also from the species of *Leishmania*, not only in their agglutination reactions, but also in ability to ferment different sugars.

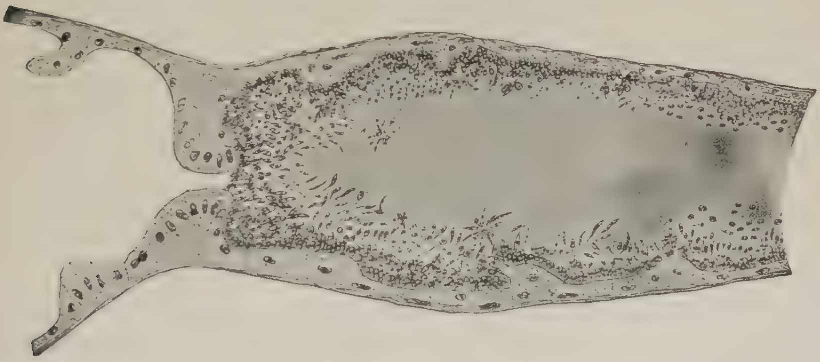

FIG. 35. Longitudinal section of the intestine of a dog flea, showing herpetomonads lining the hind-gut. × 170. (After Wenyon, "Protozoölogy.")

The genus *Leishmania* is indistinguishable from *Herpetomonas* except by the life cycle; the non-flagellated leishmania forms occur normally in the tissues of vertebrate animals; when these motionless bodies are transferred to cultures, or ingested by particular insects, they are transformed into very active flagellated organisms identical with the true insect herpetomonads. They differ, however, in inhabiting mainly the stomach, and in moving forward instead of backward in the digestive tract as they multiply. No evidence of the formation of encysted leishmania forms in the hind-gut has been obtained. *Crithidia* is a genus which includes purely insect parasites which reach the crithidial stage of development; its life cycle is practically the same as that of *Herpetomonas*, the crithidial forms being substituted for the herpetomonad forms, and likewise attached by the flagellar ends. They enter the crop as cysts, literally multiply their way through the digestive tract as crithidias, and then again encyst in the rectum prior to leaving the body, though many flagellated forms are also voided. One by one many of the supposed crithidias are turning out to be really trypanosomes. The genus *Trypanosoma* is a genus of parasites which live as trypanosomes, some also assuming a leishmania-like stage, in vertebrate blood or tissues, and go through all the phases of development in insects. Their cycles of development in insects vary considerably as will be seen in the following chapter.

Leishman Bodies and Leishmaniasis

Leishman Bodies in General. — While investigating the cause of a deadly disease of tropical India known to the natives as kala-azar or dumdum fever, Leishman, in 1903, and at about the same time, Donovan, discovered in the spleen of victims numerous little round parasites. These looked to Leishman exactly like the non-flagellated stage of a trypanosome, and he naturally took them to be developmental stages of trypanosomes, and added another terrible disease to the credit of those murderous animals. Later, however, it was found that while these little round organisms resemble a certain stage in the life history of a trypanosome, yet they never reach this fully developed form. Nevertheless it was discovered that when transferred to the intestine of certain insects, or when grown on artificial cultures, they undergo a wonderful transformation. They become elongate in form and develop a waving flagellum, assuming a form identical with the herpetomonads of insects, which had long been known. Here, however, was a vicious form of the parasite which was not content with the simple life in an insect gut, but must get some romance into its existence by adapting itself to the blood and tissues of man. There is some evidence that in addition to a few species which habitually live as vertebrate parasites, some of the typical insect forms may be versatile enough, if inoculated into warm-blooded animals, or eaten by cold-blooded ones, at least temporarily to establish themselves under the strange conditions they find there, and cause more or less local and temporary inflammation and sores, or, in the case of lizards, intestinal infections. Experimental infection of mice and other animals by inoculation of insect herpetomonads, reported by Laveran and Franchini (1913–1915) and Fantham and Porter (1915), have not, however, been confirmed by other workers.

There are two distinct kinds of *Leishmania* infections in man, which are spoken of as visceral and cutaneous. There are usually recognized two types of visceral leishmaniasis; one is kala-azar, which is a very severe and often fatal disease occurring in India, Transcaucasia, China, Sudan and possibly other parts of Africa; the other is infantile kala-azar, with which canine kala-azar is probably identical, and which occurs around the Mediterranean Sea and is largely confined to very young children. Likewise there are at least two distinct types of cutaneous leishmaniasis. One is Oriental sore, occurring from North Africa to India, in which the principal manifestation is a local and temporary sore, usually on exposed parts of the body; the other is espundia of South America, in which the skin sores may develop into ulcerating sores of very long duration which spread over considerable areas, not only of the skin, but also of mucous membranes of nose and mouth, and which not infrequently prove fatal. Other types of cutaneous leishmaniasis have, however, been described in South America, such as " uta " of Peru. These differences in clinical manifestation suggest the possibility that in South America there may be not one but several species, or at least varieties, of *Leishmania* causing them. The number of different species of Leishmania causing disease in man is a disputed point. Most workers now regard the parasites of kala-azar and infantile kala-azar as identical, but consider the parasites of Oriental sore and the South American forms of cutaneous leishmaniasis as separate species. Cross-immunity tests support these distinctions, and in Central Asia, where Oriental sore and kala-azar overlap, the two diseases occur side by side, in the same or different patients, without apparently influencing each other in any way. For the present, therefore, we may recognize three species of *Leishmania* parasitic in man: — *Leishmania donovani*, causing kala-azar; *L. tropica*, causing Oriental sore; and *L. braziliensis*, causing espundia. The possibility exists that there may be other species in South America. Many writers refer to the parasites of infantile kala-azar as *L. infantum* or *L. donovani* var. *infantum*. Young and Hertig found some difference in the course of infections in hamsters between the Mediterranean and canine strains, on the one hand, and the Indian and Chinese strains on the other, but the difference may have been due to the longer growth in artificial culture of the former strains.

Leishmania donovani and Kala-azar

One of the most important scourges of life in Bengal and Assam is kala-azar or " black sickness," a disease which is mysterious in its origin, slow in its development, and fearful in its effects. In some places whole villages have been depopulated, and populations of large areas reduced. A few decades ago the people, terrorized, often deserted their homes by hundreds, or isolated themselves from the outside world, or burned to death the unfortunate victims of the disease. Now there are numerous clinics for the diagnosis and treatment of the disease, and many thousands who would in the past have gradually wasted away and come to an almost certain early death, are now treated and cured.

Apparently since about 1875 the disease has slowly extended itself through nearly the whole of the Assam Valley, and appears to be on the increase in Assam and Bengal. Napier believes there are not less than a million cases in Bengal. It also occurs in Madras, but not in Ceylon or Burma. It is endemic in the Yangtse Valley in China and in the Anglo-Egyptian Sudan. Around the shores of the Mediterranean and in Transcaucasia the same or a similar disease occurs, but whereas in India and China kala-azar attacks young and old alike, around the Mediterranean it attacks infants and young children almost exclusively. Children between one and two years old are most often affected, while children over six years are practically exempt. A single case has been found in Brazil, contracted in a region where another form of leishmaniasis is prevalent. It is difficult to know how to explain this case.

Leishmania donovani. — The parasite of kala-azar, as it occurs in the human body, is usually a minute round or ovoid body only 2 to 4 μ in diameter (Fig. 36). It has a delicate cell membrane, and contains a rounded nucleus usually applied to one side of the body, and a kinetoplast which appears either as a minute dot beside the nucleus or as a tiny rod lying obliquely with reference to the nucleus. Torpedo-shaped parasites are also found, especially in the spleen. They multiply by simple fission; sometimes rosette-like clusters of individuals occur as the result of rapid, repeated division. These bodies are widely distributed in the body, but the special habitat seems to be the large endothelial cells of blood vessels and lymphatics; they are especially abundant in the spleen, liver and bone marrow, but are by no means confined to these organs. They are found both inside and outside of the tissue cells, and are present in limited numbers in the circulating blood, usually inside of leucocytes or, occasionally, free. Often the cells containing the parasites enlarge to many times their normal size, and may contain dozens of parasites.

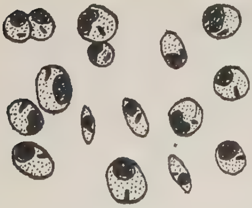

FIG. 36. *Leishmania donovani* from a smear from a leishmanoid nodule. × 1600. (After Knowles, "Introduction to Medical Protozoölogy.")

When a culture is made from the blood or spleen juice of an infected individual, the parasites undergo their remarkable transformation into active, flagellated herpetomonads (Fig. 38). Typically these are spindle-shaped, about 14 to 20 μ long and from 1.5 to 3.5 μ broad. The round or oval nucleus is in the center, and the usually oval parabasal lies transversely near the anterior end; in front of it is a light-staining area called the "eosinophile vacuole," over or around which runs the root of the flagellum. The flagellum is as long or longer than the body.

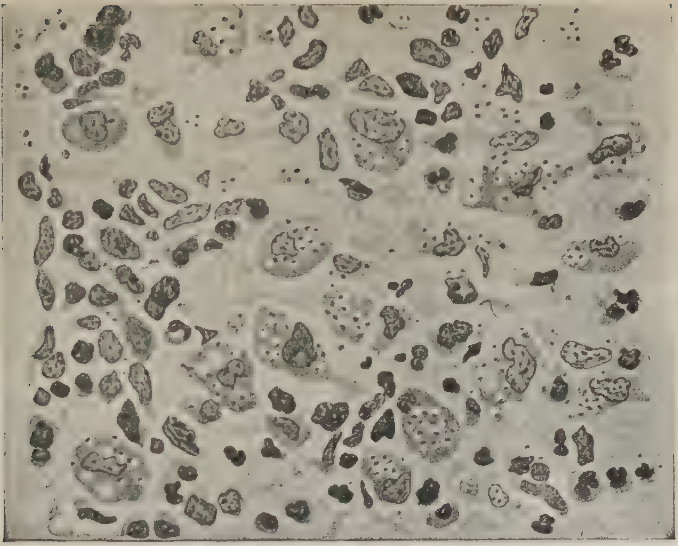

FIG. 37. Section of human spleen showing numerous leishman bodies in the cells. × 750. (After Nattan-Larrier, from Wenyon, "Protozoölogy.")

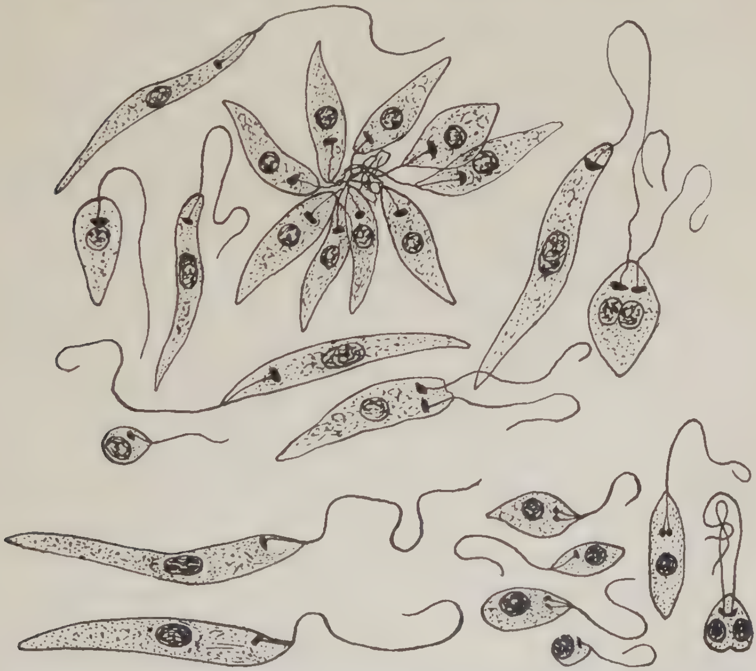

FIG. 38. *Leishmania donovani.* Upper figures, forms found in cultures. Original. Lower, forms found in mid-gut of *Phlebotomus argentipes;* at left forms found in lumen; at right forms found attached to walls. × 1600. (Sketched from figures by Shortt, Barraud and Craighead.)

The flagellates divide by longitudinal fission. In young cultures many stumpy, pear-shaped or oval forms are found, and the body tends to become relatively more slender as the culture matures. Row has described " O " bodies which he thinks are reversions of the flagellates to resistant, non-flagellated forms which are the cause of infection, but most workers believe that these are merely dying and degenerate flagellates.

Transmission. — Few problems in parasitology have caused more fruitless effort, more blasted hopes, more false conclusions, or more unfounded speculation than the transmission of kala-azar, and the end is not yet. Kala-azar is a house and site infection, and for this reason it was believed for a time that infection spread by way of contaminated soil. Then Patton (1907) discovered that the parasites transform into flagellates, and multiply as such, in the mid-gut of bedbugs. In the following 18 years Patton, Cornwall, Adie, and others endeavored to prove that the bedbug was the natural vector of kala-azar, but, as Knowles puts it, although the bedbug started as a hot favorite, it never reached the winning post. Shortt and his colleagues of the Indian Kala-azar Commission finally concluded, in 1925, that the bedbug does not transmit kala-azar either directly by its bites or indirectly by its feces. There is, furthermore, abundant epidemiological evidence which should have thrown graver suspicion on the transmission of kala-azar by bedbugs than it did. Meanwhile in the Mediterranean region attention was focused on fleas, since there dogs are commonly infected with a visceral form of leishmaniasis which was believed to be identical with the infantile disease, and fleas were the most obvious insect parasites of both children and dogs. A brief history of the work in connection with fleas and leishmaniasis is given on p. 492. The case against fleas, in both infantile and canine kala-azar, was as effectually exploded by Nicolle and Anderson, in 1924, as was the case against bedbugs by Shortt *et al.* in 1925. Many other insects, including *Triatoma*, lice, mosquitoes, *Culicoides*, ticks, etc. have been suspected, experimented with, and discarded, but one group of insects, the sandflies (*Phlebotomus*), have been found to merit most careful consideration. In the first place, the epidemiological evidence strongly suggests sandflies, as Napier has demonstrated. The disease in India is limited to areas of high relative humidity, with rare exceptions at elevations of less than 2000 feet, and to a geographical distribution which suggests a transmitting agent of limited range. It was then shown by Knowles, Napier and Smith that *Phlebotomus argentipes* becomes very easily and heavily infected when fed on kala-azar patients. Subsequently this work was confirmed by the Kala-azar Commission and full details of the developmental cycle in the sandfly worked out, with the demonstration of massive infections of pharynx and mouth cavity, whence the flagellates must inevitably be inoculated into the skin when the insect is biting.

This experimental evidence, together with the almost perfect accord of the sandfly transmission theory with the facts of distribution in India, make it difficult to believe that the solution has not been found. But it is still a fact that, in spite of the most persistent efforts to actually transmit kala-azar by the bites of sandflies, either to man or animals, no one has yet succeeded. In China, although Hertig, Young, and others have shown that Chinese sandflies, also, become infected, the epidemiology does not support the case against the sandflies quite so well (see p. 513). Is the sandfly work, so full of promise at the beginning, to prove as futile as the work with the bedbug and the flea?

In nature kala-azar occurs only in man and in dogs, and in dogs it is limited in its geographic distribution to the Mediterranean and Transcaucasian regions, over much the same area as the infantile type of kala-azar. The distribution of these two infections agrees in a general way but not in detail. There are many localities where both occur together, but there are others where only one or the other is common. Interestingly enough a similar situation exists with respect to cutaneous leishmaniasis in dogs — it occurs in practically the same areas as human Oriental sore. In Transcaucasia, where the two human diseases overlap, the same is true of the canine diseases. Since *Leishmania donovani* can be inoculated into dogs, the Mediterranean strain more easily than the Indian, and since there is no evident difference in the parasites, the disease, or the geographic distribution, it seems reasonable, as Wenyon suggests, to regard both man and dog as susceptible, the transmission very likely being by the same vector, presumably a sandfly, in either case. The greater local frequency of the infection in one host or the other may be due to environmental factors which affect the feeding habits of the vectors, or relative frequency of exposure to their bites. It frequently happens, however, that human and canine cases have been closely associated, and Basile (1916) states that in one locality in Sicily where there were many infected dogs, extermination of these led to an almost complete disappearance of the human disease.

L. donovani infections can also be transferred to monkeys, mice and Chinese hamsters (*Cricetulus griseus*), but only by means of relatively large doses of organisms, obtained either from infected spleen juice or from cultures. Cultures are not infective until the fifth and usually the seventh day, when the flagellates are numerous. Experimental animals often show no symptoms even when very heavily infected.

The Disease. — Although kala-azar was long thought to be practically 100 per cent fatal when untreated, this has been found not to be true.

Observations in Calcutta suggest that there may be many latent cases in whom, although the parasites are present, the disease may not develop. Knowles (1928) says that the onset of kala-azar is likely to be one of three types, — typhoid-like, malaria-like or dysentery-like. Not only is it *like* these diseases, but it begins with actual cases of them, and the conclusion seems almost unavoidable that infections with typhoid, malaria, dysentery or other diseases actually precipitate kala-azar in patients who were presumably already infected. McCombie-Young has noted a special tendency for kala-azar to become epidemic after a series of unhealthy years; a marked increase of the disease in Assam occurred from 1919 onwards, following the great influenza epidemic.

After the onset an irregular fever persists for several weeks. Meanwhile the spleen and liver enlarge enormously, increasing and decreasing with the fluctuations of the fever. After several weeks the fever drops and the patient becomes almost normal for some time, only to be attacked by the fever again, with an enlargement of spleen and liver. These remittent attacks gradually dwindle to a steady low fever, accompanied by sweating spells, rheumatism-like aches, high pulse rate, anemia and a general wasting away, with the skin often a dark earthen color. Dysenteric symptoms, with discharges of blood and mucus, are common, especially in the late stages of the disease, and frequently after death the intestine is found to be extensively ulcerated, with numerous parasites in the walls of the ulcers. Parasites are usually found most abundantly in the spleen, liver capillaries, bone marrow and lymph glands. When the chronic condition is reached the patient presents an appearance not unlike that resulting from chronic malaria, and it is little wonder that the diseases were long confused. Usually complication by some other disease, especially dysentery, which gets a severe hold on account of the low vitality of the victim, causes death (according to Rogers in 96 per cent of cases), but in a relatively small per cent of cases there is recovery. A steady gain in weight, however slight, is said by Mackie to be a fairly accurate sign of recovery.

An interesting phase of the disease is the development of skin nodules, a condition known as " dermal leishmanoid." It usually develops in patients who have had kala-azar, have been treated, and have recovered. The nodules, which are entirely unlike Oriental sore, contain the parasites, but cultures of the peripheral blood are negative and the spleen is not enlarged. Apparently the parasites are able to localize in the skin after the blood and viscera have become too " hot " for them.

Diagnosis. — In earlier days kala-azar was often confused with chronic malaria, and many a patient has endured, or perhaps failed to endure, long courses of antimony injections when he should have had quinine, and vice versa. There is no longer any excuse for such mistakes, for the laboratory diagnosis of kala-azar is now established on a very firm basis. Shortt *et al.* have shown that over 75 per cent of kala-azar cases can be diagnosed by examination of blood films, either " thick films " which have been dehemoglobinized, or better still the thick edge of a film, left when a slide used for making the smear is lifted off just before the blood is exhausted, in which will be found the majority of the leucocytes. The most certain method of diagnosis, however, is by spleen puncture, which, if properly done on the enlarged spleens of kala-azar cases, is easy and safe. The extracted spleen juice is used both for a smear and for inoculation of a culture. About 90 per cent of cases can be diagnosed, most of them very rapidly, by the smear, and practically 100 per cent by the culture.

Since kala-azar infections produce profound changes in the blood serum, it is possible to use tests for kala-azar which are comparable to the Wasserman and Kahn tests in syphilis, though of different nature. One of these is Napier's aldehyde test, in which a drop of strong formalin is added to 1 cc. of serum. In kala-azar cases the serum gels *and turns milky white;* a mere gel is not diagnostic. This test appears to be perfectly specific, and seldom fails; many unsuspected infections have been brought to light, and subsequently proved by culture of the spleen juice. An even more accurate test is the antimony-serum test, in which a permanent flocculent precipitate is formed at the line of junction of a layer of serum and a layer of a solution of urea stibamine or similar antimony compound.

Treatment. — Since 1914 the remarkable destructive effect of antimony, especially in the form of tartar emetic, on Leishman bodies has been thoroughly established. Tartar emetic as a cure for Leishmanian diseases was first tried out in 1912 with astonishing success by Vianna, a Brazilian investigator, on the Leishmanian ulcers of the face and nasal mucosa. Similar treatment has been applied with equal success to other forms of leishmaniasis. Its application to kala-azar has been attended with great success, and even advanced stages of the disease can sometimes be cured by the use of this and related antimony compounds. Sodium antimony tartrate is used most extensively, but the pentavalent compounds such as urea stibamine and " Von Heyden 471 " are effective in fewer injections, though much more expensive.

The usual method of giving tartar emetic is by intravenous injections, the dose being gradually increased in accordance with the age and tolerance of the patient. The drug is a powerful one, and if given in overdoses may cause severe disturbances of the digestive tract and of the kidneys, but if it is given in small quantities to begin with, and its effects carefully watched as the doses are increased, it can be used without danger, and constitutes a treatment as specific in its effects as is quinine on malarial parasites, or salvarsan on spirochætes.

Prevention. — On account of the uncertainty which exists concerning the mode of transmission of kala-azar, nothing very definite can be said about its prevention. The probability of transmission by sandflies suggests avoidance of infected houses and infected people after dusk, when the flies begin biting. Disinfection of likely breeding places in and near the houses to destroy the larvæ would probably be possible in many instances, but the safest method is to burn or destroy the native huts and outhouses with all their junk and prevent the erection of a new hut on the same site. This method of coping with the disease before it has had time to spread has been successfully used on some of the tea estates in Assam. An isolation of a few hundred yards is quite adequate to prevent the spread of the disease, a fact which is in accord with the sandfly transmission theory. Where cows are kept on the ground floor of huts, or in a shed adjoining it, as frequently happens, the sandflies attack the cattle in preference to man, but the presence of the animals attracts the insects, hence protection by keeping cows in close proximity is not unattended by danger. The possibility of controlling the disease locally by the establishment of a free clinic and treatment of all cases is now under investigation. In endemic regions where the canine disease occurs, dogs showing the slightest symptoms of feverishness, enlarged spleen or emaciation should be killed, but even if this were done it would not necessarily stamp out the disease completely, since so many dogs carry the infection in latent condition, serving as a reservoir for it without showing any appreciable symptoms. Basile showed the value of attacking the disease in dogs by destroying all obviously infected dogs in a certain township in Sicily. In the year the dogs were destroyed there were seven new cases of the disease in children in a population of 2000, but in the following year not a single new case appeared, and in the year after only one.

Oriental Sore

One of the commonest sights in many tropical cities, particularly in the cities of the eastern Mediterranean region and southwestern Asia, is the great number of children, usually under three years of age, who have on the exposed parts of their bodies unsightly ulcerating sores, upon which swarms of flies are constantly feeding. In some cities infection by these parasites is so common and so inevitable that normal children are expected to have the disease and visitors to the cities seldom escape a sore as a souvenir, even if present for only a short time. In Bagdad, Wenyon has shown that almost as soon as the children are relieved of the wrappings in which they are covered as babies, and allowed to run free and play in the streets, they are almost certain of infection. Since one attack gives immunity, Oriental sores appearing on an adult person in Bagdad brands him as a new arrival, and the same is undoubtedly true in many other tropical cities. The disease is more or less prevalent all around the shores of the Mediterranean, through Syria, Arabia, Mesopotamia and Persia to Central Asia and the drier parts of Central and Western India, and also in many places in Central Africa. It is possible that true Oriental sore has been introduced into South America also, but here it is obviously difficult to distinguish it from the native South American espundia, which, in fact, some parasitologists believe is caused by the same parasite.

The parasite of Oriental sore, *Leishmania tropica*, is morphologically indistinguishable from *L. donovani*, either in lesions or in cultures, but it differs immunologically, as Noguchi (1924) demonstrated. The clinical effects are totally different, and one infection does not protect against the other.

The parasites are found in the tissues of the sores, in which many large cells, probably derived from the reticulo-endothelial system, are literally packed with them. It is doubtful if they occur outside the cells except as a result of their rupture. Torpedo-shaped parasites (Fig. 39) are more commonly found than in kala-azar. Growth in culture is identical with that of *L. donovani*, and cultures can be kept going indefinitely by subinoculation.

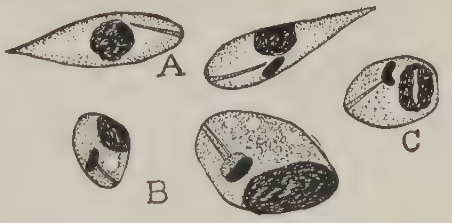

FIG. 39. *Leishmania tropica* from an Oriental sore; *A*, torpedo-shaped forms found outside the cells; *B* and *C*, intracellular forms. × 4000. (After Wenyon.)

The Disease. — Oriental sore begins as a small red pimple, like an insect bite, but instead of fading away it persists for a year or so, and grows until a raised nodule an inch in diameter is formed. The surface of the nodule is covered by red granulations which bleed readily. The sores may be slightly itchy at first but are never painful. Eventually a scab forms, and when this falls off a thin depressed scar is left. More often, though, the sores become contaminated and ulcerate; the ulcers may get as large as the palm of the hand. In these cases the parasites are not so easily found, and usually have to be sought in the surrounding red rim of the sore. The sores usually form on exposed parts of the body, and, as Acton first observed, in those places most frequently attacked by sandflies, — on the back of the wrist, between the fingers and toes, on top of the foot, or on the face, arms or legs. Usually there is only one sore, but two or three are common, and there may be many. Sometimes neighboring lymph glands become enlarged and contain parasites, but constitutional symptoms are rare in spite of the fact that a permanent immunity is usually conferred. Some workers believe that mild constitutional effects are present, especially during the incubation period, but are generally overlooked.

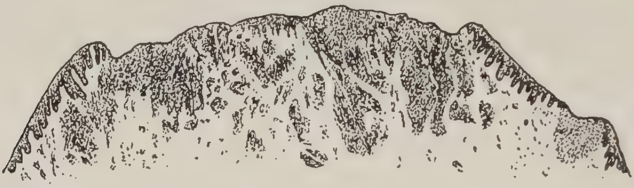

FIG. 40. Section through an Oriental sore, showing loss of epithelium, and accumulation of large cells (macrophages) represented by dark areas. These cells are heavily laden with Leishman bodies. Sketched from Nattan-Larrier in Wenyon's "Protozoölogy."

In the regions where Oriental sore prevails, dogs frequently suffer from similar lesions, especially on the nose and ears. It is the general opinion that the dog infections are caused by the same parasite as those of man, since dogs inoculated from human Oriental sores develop identical lesions. Other animals, such as cats, monkeys, rats, mice, and guinea pigs can sometimes be inoculated successfully; in mice generalized infections, in many respects resembling kala-azar infections, result from intraperitoneal injections, but skin lesions usually appear also.

Transmission. — As in the case of kala-azar, the transmission of Oriental sore has long been a baffling problem. Much of the difficulty seems to have been due to failure adequately to study and consider epidemiological facts.

The possibility exists of contamination of abraded skin with material from an Oriental sore, by direct contact, by towels or bed linen, or by house flies, but it is doubtful if this accounts for more than a very few cases. Transmission by biting insects is much more probable, especially in view of the seasonal incidence of the infection. As in the case of kala-azar, the bedbug, nearly always the first insect to be picked on as a transmitter, was early incriminated because Wenyon (1911) and Patton (1912) showed that *L. tropica*, like *L. donovani*, goes through the flagellated stage in its stomach, but subsequent work has given little balm to the believers in bedbug transmission. Fleas, lice and mosquitoes were all placed on trial, and all acquitted.

The case against sandflies (*Phlebotomus*) is better founded. After a number of unsuccessful attempts, due probably to the use of the wrong kinds of sandflies or attempts to inoculate immune people, Sergent *et al.* (1921) first succeeded in causing infection in Algiers, where the disease is not endemic, by rubbing infected sandflies, sent from Biskra, into the scarified skin of a volunteer, and this was followed by similar successes by a number of other workers. In 1920 several French workers in Algeria discovered that the gecko, *Tarentola mauritanica,* harbored a similar herpetomonad parasite, and since sandflies (*Phlebotomus minutus*) feed ravenously on this lizard, the suggestion was made that the sandfly transmitted it. The failure of *P. minutus* to bite man later took the wind out of the sails of the gecko reservoir theory, but the matter is not yet closed, for Young and Hertig have shown that the gecko flagellates (called *L. tarentolæ*) produce visceral infections in hamsters similar to those produced by the Mediterranean type of *L. donovani,* and Strong (1924) recorded a remarkable series of events which, if confirmed, are of far-reaching significance. In Panama, he observed that Euphorbia plants were extensively infected with a herpetomonad. Certain bugs, after feeding on the plant, became infected. Lizards fed on the bugs and similar parasites occurred in their intestines. Parasites from plants and bugs, when inoculated into animals, produced no effect, but the lizard parasites, inoculated into the skin, produced a cutaneous infection.

Adler and Theodor have continued the sandfly work, and have shown that a fair percentage of *Phlebotomus papatasi* and *P. sergenti* fed on Oriental sores develop the infection, which follows a course similar to that of *L. donovani* in *P. argentipes;* that natural infections of these sandflies occur; that infected flies when rubbed into the skin produce infection; and that these flies can infect a culture medium by biting through a membrane. The evidence against the sandflies is, therefore, very strong, but the crucial test — transmission by the bites — has not yet succeeded. Transmission by crushing flies into bites made by them is, however, definitely proved. The question of the species of sandflies involved, and a discussion of them, will be found on p. 511.

It is, of course, possible that other insects as well as sandflies may be involved in the transmission of cutaneous leishmaniasis. Gachet (1915) thinks that the wingless fly, *Hippobosca canina,* which is very abundant on dogs in Teheran, may be involved in the transmission of canine leishmaniasis there.

Treatment and Prevention. — The best treatment for Oriental sore is the same as for kala-azar, — intravenous injections of antimony compounds. This sets up a local inflammation, the parasites disappear from the sore, and the sore heals in 15 to 30 days. Local treatment of the sore with X-ray, CO_2 snow, methylene blue ointment, etc., have a favorable influence, but are not as effective as the antimony injections.

Control probably lies largely in keeping the sores, on either man or dog, protected so that sandflies, or any other biting insects, cannot get at them, for it is not likely that insects can get infected from sucking blood elsewhere, since blood cultures are never positive.

American Leishmaniasis

In many parts of Brazil, Paraguay, Bolivia, Venezuela, French Guiana, and other countries of tropical South America, there occurs a horrible form of Leishmanian ulcers which are not always content to attack only the skin, but in a percentage of cases attack also the mucous membranes of the nose and mouth cavity. Such ulcers do not grow to a limited size and then heal, but slowly and constantly spread farther and farther, lasting for a period of five, ten, fifteen or more years. The disease goes by a great variety of local names of which espundia is the most common. The best name of all is probably "American leishmaniasis." The name "buba braziliensis" has been given it by some writers, but erroneously, since this name properly belongs to another tropical disease, yaws. A few cases of *Leishmania* ulcers have been observed in dogs in South America. Monkeys can be experimentally inoculated.

The organism causing these intractable ulcers, *Leishmania braziliensis*, does not differ in any morphological details from the Old World species of *Leishmania*, either in the lesions or in cultures, but, aside from the difference in clinical effects, they have been shown by Noguchi to differ in their immunological reactions.

However, it is by no means certain that only a single type of leishmaniasis occurs in South America. It is possible that the true Old World Oriental sore may also have established itself in various places in South America, if a suitable insect transmitter occurs there. Townsend (1915) thinks there is little reason for supposing that the mild Leishmanian infection known as "uta" on the western slopes of the Peruvian Andes is identical with the severe "espundia" at the low-lying forests of Brazil.

Skin Sores. — The sores on the skin, which do not always ulcerate, usually begin as one or two itching spots that seem to be produced by the bites of insects. If the sores are of the non-ulcerating type there is produced a great deal of red granular tissue, raised slightly above the surrounding skin, and bleeding easily. The surface, which is rosy in color, is rough, resembling, according to one author, a cauliflower. An intolerably foul-smelling fluid is constantly emitted which sometimes dries over the sore to form a crust of varying thickness. The fluid given off is infectious and starts new sores if it comes in contact with any broken skin on the same or another individual.

In the ulcerating type of the disease in the skin the same fetid fluid is emitted, but instead of the sore being elevated, it is extensively excavated and has raised borders. Often an enclosing crust forms over it and it is improperly called a "dry sore." In this case the fluid is shut in between the crust and the sore and causes even more intensive destruction of the tissues. Sometimes nearby lymph glands also become infected. Such general symptoms as evening fever, pains in the joints, headache, etc., sometimes accompany the ulceration, probably due to the absorption of toxins.

As remarked before, the exudations from the sores are extremely infectious for either the same individual or another one. Consequently it is not infrequent to find on a single individual a great many sores, up to 50 or more, in all stages of development, though more often there are only a few. In one case recorded from Brazil there were 35 active sores and 29 extinct ones, and these were arranged in a more or less symmetrical manner, suggesting the influence of the nervous system on their location. The sores become secondarily infected with bacteria and spirochætes and are sometimes attacked by screw-worms and other fly maggots. The rarity of Leishman bodies in the late stages of the sore suggests that the secondary infections may then play an important rôle, though the prompt cure which follows treatment destructive to the protozoans shows that the latter still play a leading part.

Mucous Membrane Ulceration. — A far more vicious manifestation of the disease and one which follows the cutaneous sores is the ulceration of the mucous membranes of the nose and mouth (Fig. 41). It may be several months or over a year after the skin sores develop, and often after they have healed, that the mucous ulcerations appear. In rare cases ulcers have been known to occur in the vagina also. Ordinarily the infection commences as a tiny itching hardness or swelling of the mucous membrane, usually in the nose, the infected membrane becoming inflamed, and marked either with small granular sores or with blister-like swellings. The lymph glands in the infected regions become swollen and turgid. A granular ulceration begins in a short time, invading all the mucous membranes of the nose and spreading, by means of infective fluid which flows down over the upper lip, into the mouth cavity, attacking the membranes of the hard and soft palate. Its advance is obstinate and slow, and gives rise to serious complications.

The nostrils become too clogged to admit the passage of sufficient air and the patient has to keep his mouth constantly open to breathe. His repulsive appearance and fetid breath help to make his life miserable. Affections of the organs of smell and hearing, and even sight, often supervene, and the voice is weakened or even temporarily lost. The digestive tract becomes upset from the constant escape down the throat of the exudations from the ulceration, mixed with saliva or food. A spreading of the nose due to the eating away of the septum is a characteristic feature. Although in late stages of the disease the entire surface of the palate and nasal cavities is attacked, and the septum between the nostrils destroyed, the bones are left intact, a feature which readily distinguishes a Leishmanian ulcer from a syphilitic one. Usually the victim of espundia, after long suffering, sometimes for 20 or 30 years, succumbs to the disease from pure exhaustion and from poisoning by exuded liquids which are swallowed.

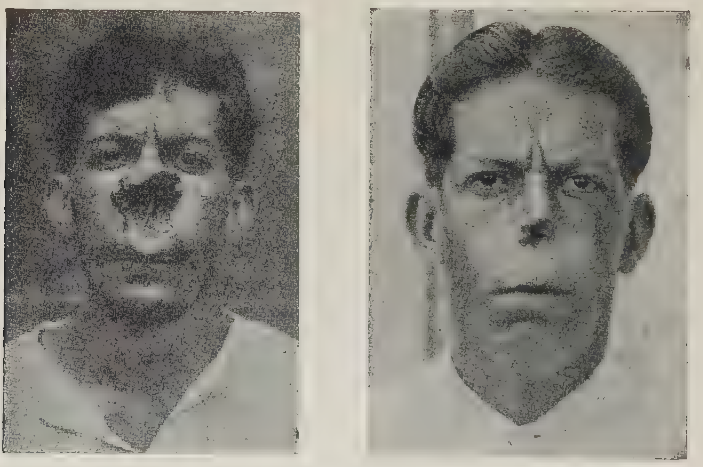

FIG. 41. A case of espundia before and after treatment with tartar emetic. (After d'Utra e Silva.)

Transmission. — Very little can be said on this subject. In some places it is claimed by the natives that the disease is contracted in the forests in the daytime, on exposed parts of the body, which would throw suspicion on tabanids or simuliids. Natives of Paraguay believe that rattlesnakes harbor the parasites and that the latter are transmitted to man by sandflies, black flies or ticks, all of which attack the snakes. Although only a popular belief, this is interesting in view of the suspicion attached to geckos as reservoirs of *L. tropica* in Algeria.

By analogy with the Old World leishmaniasis, it seems most probable that sandflies are involved in the transmission of espundia. Instances are recorded of typical sores developing on the site of bites of *Phlebotomus lutzi*. Aragão (1922) found herpetomonads in some wild *P. intermedius* captured in a locality in Rio de Janiero where a local outbreak of about 50 cases followed the arrival of an infected individual, and in five of these flies, fed on espundia sores three days before, he found similar flagellates; when emulsions of the flies were inoculated into the nose of a dog, an ulcerating sore containing *Leishmania* developed three months later.

In the case of the strain of uta found in the Peruvian Andes, Townsend (1915) obtained good experimental evidence that two species of midges of the genus *Forcipomyia* (see p. 518) were the transmitters. Inoculation of the gut contents of these insects into guinea pigs produced sores believed to be identical with uta, and Townsend thinks the insects transmit the disease in nature by voiding the Leishman bodies from the anus, the puncture being contaminated in this way. This does not, however, correspond with the cycle of development of other species of *Leishmania* in insects. It seems altogether impossible, however, aside from any experimental evidence, that a disease occurring in the canyons of the Andes, over a mile above sea level, could be transmitted by the same insect as in the steaming, marshy forests of the Amazon Valley. The sandflies of the mountain slopes have been carefully investigated in connection with Oroya fever, and no evidence of their complicity in the transmission of " uta " has come to light.

Treatment of espundia with antimony is quite as successful as in other Leishmanian diseases, and even more spectacular. It was in connection with this disease that its effectiveness in leishmaniasis was first discovered by Vianna. Little can be said about prevention until the methods of transmission are more definitely established, although Aragão's success in stopping the local outbreak in Rio de Janiero by screening of infected cases is very suggestive.

CHAPTER VIII

HÆMOFLAGELLATES — II. TRYPANOSOMES

One of the blackest clouds overhanging the civilization of tropical Africa is the scourge of trypanosome diseases which affect both man and domestic animals. The destiny of equatorial Africa depends largely on the issue of the struggle of science against these haunting maladies. The ravages of sleeping sickness, which is the final phase of trypanosome infection in man, were well known to the old slave traders, and the presence of " lazy niggers " lying prostrate on wharves and docks with saliva drooling from their mouths, insensible to emotions or pain, was a familiar sight. It did not take these astute merchants long to find that death was the inevitable outcome of the disease, and they very soon recognized swollen glands in the neck as an early symptom and refused to accept as slaves negroes with swollen glands. Nevertheless sleeping sickness must often have been introduced with its parasites into various parts of North and South America, as it frequently is even at the present time, and only the absence of a suitable means of transmission has saved the Western Hemisphere from being swept by it. Fossil remains of tsetse flies have been found in Colorado, belonging to the oligocene period, and it has been suggested that the extinction of prehistoric camels and horses in North America, which cradled them in the early days of their evolution, may have been brought about by tsetse-borne trypanosome diseases.

Although trypanosomes were first discovered in 1841, which is very ancient history in parasitology, the first connection with disease was the discovery of their responsibility for " surra " in horses and other animals in India in 1880. In 1895 Bruce showed that " nagana " of domestic animals in Africa was caused by a trypanosome which now bears his name. In 1902 Forde and Dutton discovered the presence of trypanosomes in human blood in a case of " Gambia fever " which is now known to be the preliminary stage of sleeping sickness. In 1903 Castellani found trypanosomes in the cerebrospinal fluid of cases of sleeping sickness in Uganda. The transmission of nagana by tsetse flies was known even before the cause of the disease was discovered, but it required the labors of many workers to elucidate the details of the process. It was Kleine, in 1909, who showed that the tsetse fly was no mere mechanical transmitter, but a true intermediate host. In that same year there was discovered a new type of human sleeping sickness in Rhodesia, and Chagas described an entirely different human trypanosome infection in South America.

The Parasites. — The general relationships of trypanosomes have been discussed on p. 119. They may be regarded as having developed in the course of evolution from the crithidias of invertebrates, which have adapted themselves to living in the blood of vertebrates on which the invertebrates habitually feed. They thus bear the same relation to *Crithidia* that *Leishmania* bears to *Herpetomonas*.

Trypanosomes live as parasites in all sorts of vertebrates, — fish, amphibians, reptiles, birds, and mammals, — living in the blood, lymph, or tissues of their hosts. A great number of different species have been named; usually any trypanosome found in a new host is named after the host as a sort of tentative label, until more is found out about it. While this procedure is not in accordance with rules of naming animals, it is better than the alternatives of having numerous nameless trypanosomes to deal with, or of identifying them with species from which they may subsequently be found to differ. Since only a few trypanosomes can be recognized by their appearance, they usually have to be identified by their behavior. They differ in their agility; in their pathogenicity for different animals, and the nature of the infections they set up; in their development in cultures; in the invertebrates in which they undergo development, and more especially in the course the development takes; and, finally, in their immune reactions.

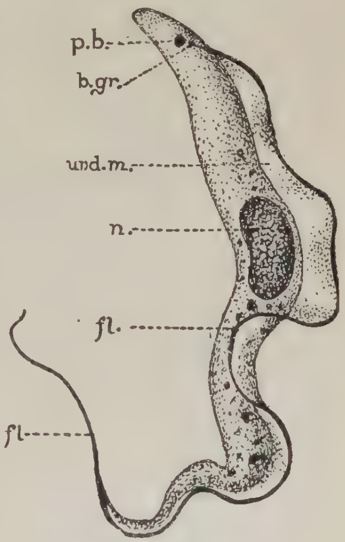

FIG. 42. *Trypanosoma gambiense*, slender form. *p. b.*, parabasal body; *b. gr.*, basal granule; *und. m.*, undulating membrane; *n.*, nucleus; *fl.*, flagellum. × 4000.

In form most trypanosomes are very active wriggling little creatures somewhat suggesting diminutive dolphins or eels, according to their slenderness. They swim in the direction of the pointed end of the body, being propelled by the wave motions of the undulating membrane. Some of them dart in and about among the blood corpuscles with great rapidity, while others wriggle in a more leisurely manner. The body is shaped like a curved, flattened blade, tapering to a fine point anteriorly, from which a free flagellum often continues forward. This flagellum continues to near the posterior end of the body, and is connected with the body along the " back " by an undulating membrane, like a long fin or crest, which in some species is thrown into numerous graceful ripples, while in others, *e.g.*, *T. lewisi*, it is only slightly rippled. The body contains a nucleus which varies in its position in different species and under different circumstances. Near the posterior end, or sometimes at the tip, there is a parabasal body (rarely absent) and a basal granule from which the flagellum arises. Many species also contain scattered, deep-staining granules in the cytoplasm.

Life Cycles. — In the vertebrate hosts trypanosomes may multiply either by simple or multiple fission. In *Trypanosoma gambiense, brucei, lewisi*, and many others, there is a simple longitudinal division of the parasites in the blood which results in the presence of long slender forms, short stumpy ones with no free flagellum, and intermediate forms. Such trypanosomes are therefore spoken of as polymorphic. In the case of *T. lewisi* of rats the host, after a few days, develops a special type of antibody which does not injure the parasites but inhibits their reproduction; the result is that while *T. lewisi* is very polymorphic in the first few days of infection, after about ten days there is no more reproduction and the parasites are practically all alike. In the case of the so-called polymorphic group of African trypanosomes, to which the sleeping sickness parasites belong, no inhibition of reproduction occurs, so they are always polymorphic. Other species, such as *T. cruzi* of South America, and many others, such as *T. evansi* causing surra, *T. equiperdum* causing dourine, etc., are monomorphic in their natural hosts, though some of them are polymorphic when injected into laboratory animals. In the case of *T. cruzi*, multiple fission occurs inside the cells of the host, with the production of nests of Leishmania-like forms which then transform into trypanosomes, and broods of new trypanosomes are constantly being set free to invade other cells, but some of these get into the blood stream. It is possible that the other monomorphic trypanosomes also normally live and multiply outside the blood stream, in lymph channels or tissues, and are only secondarily found in the blood. Watson (1920) found good evidence for this in the case of *T. equiperdum*.

Although at least one trypanosome, *T. equiperdum*, has become completely independent of its ancestral invertebrate hosts, and is transmitted directly from horse to horse during copulation, and although other trypanosomes can live and multiply indefinitely in vertebrate hosts if artificially injected by the soiled proboscis of biting flies, the majority of them, when they reach a suitable invertebrate host, hark back to the traditions of their remote forebears, and go through a cycle of development more or less like that of typical crithidias. Some, like *T. cruzi* and *T. lewisi*, finding themselves in the ancestral home, as it were, revert almost completely. After being sucked into the stomach of an insect they assume the crithidial form, attach themselves to the epithelial cells or enter them, and multiply. Gradually they move backwards towards the rectum, and the infective forms are voided with the feces. Infection occurs either by infection of the bite with the feces, which is probably the usual way in *T. cruzi;* by ingestion of the feces of the insect when licking the bites, as in the case of *T. lewisi;* or by ingestion of the whole insect. In the case of *T. cruzi* the reversion to the crithidial

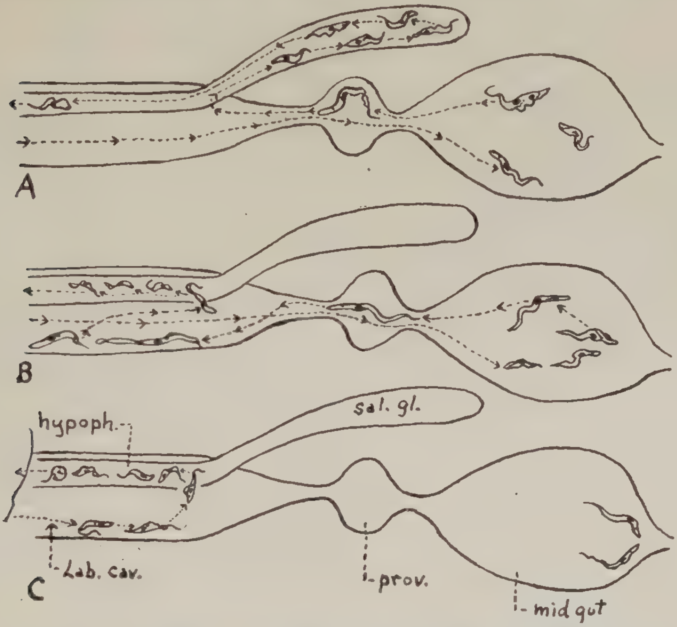

FIG. 43. Courses of development of trypanosomes in tsetse flies.

A. *T. brucei* and *gambiense.* (1) multiplication in mid-gut with development of trypanosome forms; (2) long slender trypanosomes in proventriculus; (3) passage to salivary glands and development there of crithidial and then infective trypanosome forms; hypopharynx and labial cavity used for passage only.

B. *T. congolense.* (1) Multiplication in mid-gut with development of longer slender trypanosomes; (2) long slender trypanosomes in proventriculus; (3) passage to labial cavity and development there of ribbon-shaped fixed crithidiæ and free pre-infective trypanosomes; (4) passage to hypopharynx where trypanosomes become infective and accumulate.

C. *T. vivax.* (1) Multiplication in labial cavity with production first of short crithidiæ and then pre-infective trypanosomes; (2) passage to hypopharynx where trypanosomes become infective and accumulate. Trypanosomes passing to mid-gut disintegrate. (After Lloyd and Johnson.)

condition is still more complete in that the infection commonly passes from insect to insect.

Those trypanosomes which develop thus in the hind-gut of invertebrates are said to develop in the posterior station; they are the conservatives. The trypanosomes of this group use a variety of invertebrates as intermediate hosts; for example, *T. lewisi* of rats develops in fleas, *T. melophagium* of sheep in sheep ticks (keds), *T. theileri* of cattle in tabanids, and *T. cruzi* of man and other animals in Reduviid bugs. There are other trypanosomes, however, the radicals, which after ingestion by their insect vectors develop in the anterior part of the alimentary canal and infect by way of the proboscis; so far as known at present this specialized procedure occurs only in tsetse flies, which serve as transmitters of African mammalian trypanosomes, and in leeches, which transmit the trypanosomes of aquatic animals. These trypanosomes are said to develop in the anterior station. The course of development in tsetse flies, as Lloyd and Johnson (1924) showed, is not always the same. *T. gambiense* and the other African polymorphic trypanosomes multiply first in the stomach, then pass forward to the proventriculus and labial cavity, enter the salivary duct and then the glands, multiply again, finally producing the infective forms (Fig. 43*A*). In *T. congolense* the stomach stage is followed by multiplication in the labium instead of in the salivary glands, and the hypopharynx is invaded from the labial cavity (Fig. 43*B*). In *T. vivax* the forms in the stomach die and pass out of the picture, the whole cycle taking place in the labial cavity and hypopharynx (Fig. 43*C*).

Pathogenicity and Immunity. — The very name trypanosome suggests deadly disease, yet at least the majority of trypanosomes are harmless to their hosts. Wenyon (1926) goes so far as to say: "As a general statement, it is safe to regard all trypanosomes as non-pathogenic to their natural hosts." The so-called pathogenic trypanosomes of man and domestic animals he regards as owing their injuriousness to their being in unnatural hosts; in the wild game animals of Africa, which he regards as the natural hosts, they are harbored without ill effects. The most recent evidence, however, makes it appear possible that man is actually the true host of *T. gambiense*, and that there is no reservoir of this parasite among the African game animals. Perhaps *T. gambiense* is in a unique position; it undoubtedly has arisen from a *T. brucei*-like ancestor and may have adapted itself to man sufficiently to lose its infectiveness for game animals, but has not yet reached a stage of equilibrium with its new host where it can exist without creating a disturbance. It is significant that in parts of Africa where human infections have existed longest the disease tends to assume a mild chronic form. The harmlessness of trypanosome infections is not due to any innate benignity on the part of the parasites, but rather to the power of the natural hosts to develop various means of defense, as Taliaferro (1926) clearly shows (see p. 20).

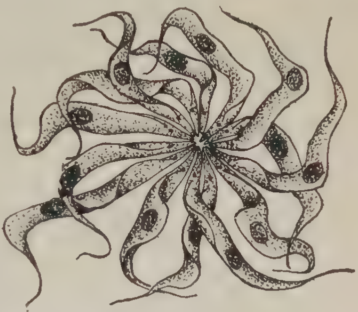

Fig. 44. Agglomeration of trypanosomes, *T. lewisi*, in blood of immunized rat. (After Laveran and Mesnil.)

It is well known that the serum of animals which have recovered from a trypanosome infection is protective against that particular trypanosome, and also that the blood of naturally immune or refractory animals (*e.g.*, sheep blood in the case of *T. gambiense*) protects against infection when injected with the particular trypanosome, though not itself trypanocidal *in vitro*. Immune blood shows various peculiar features. It can completely inhibit reproduction, or it can destroy the trypanosomes present and dissolve them; it may cause them to clump together in rosettes (Fig. 44); it may cause them to become attached to leucocytes; it may cause blood platelets to adhere to them; and it causes fixation of complement (see p. 17) when mixed with trypanosomes.

African Trypanosomiasis and Sleeping Sickness

At present three species of trypanosomes cause infection in man, two in Africa and one in South America. The African species are *Trypanosoma gambiense* and a race of *T. brucei* which was originally named *T. rhodesiense*, and which for convenience we may refer to under that name. Both these species belong to a group of closely related forms known as the African polymorphic trypanosomes.

Trypanosoma gambiense

Human infection with *T. gambiense* occurs in a wide area in tropical West Africa from Senegal to Loanda, extending inland along the rivers. It is believed that the afflicted areas have been greatly extended in recent years by the opening up of Central Africa by whites, and the consequent movement of infected natives to previously uninfected regions. The great explorer, Stanley, in his expedition to reach Emin Pasha, is thought to be responsible for the introduction of the scourge into Uganda and the Great Lakes in 1888, where, in virgin territory, it gave rise to a terrible epidemic, which in one district reduced the population from 300,000 to 100,000 in the course of seven years, from 1901 to 1908, and there are records of whole villages and islands being depopulated.

Trypanosoma gambiense varies in length from about 15 to 30 μ, with exceptionally longer or shorter forms, and shows the slender, stumpy, and intermediate types in any single blood smear (Fig. 45). The nucleus lies near the center of the body and the kinetoplast near the posterior end. The undulating membrane is only moderately rippled. When injected by the bite of a tsetse fly the trypanosomes seem to establish themselves in the lymphatic system rather than the blood, and are carried to the nearest lymph glands, which become enlarged and act as a filter. The parasites are always scanty in the blood of man, and often can only be found by inoculation of blood into a susceptible animal, or by growth in culture. They are more easily found by puncturing an enlarged lymph gland, and they are, in fact, primarily parasites of the lymphatic tissues and vessels rather than of the blood. They also invade the spleen and cause it to enlarge. Their appearance in the blood is more or less periodic. Sooner or later they invade the cerebrospinal fluid and even the brain substance. Throughout the infection, however, they appear to live between the cells, and are only found inside the cells

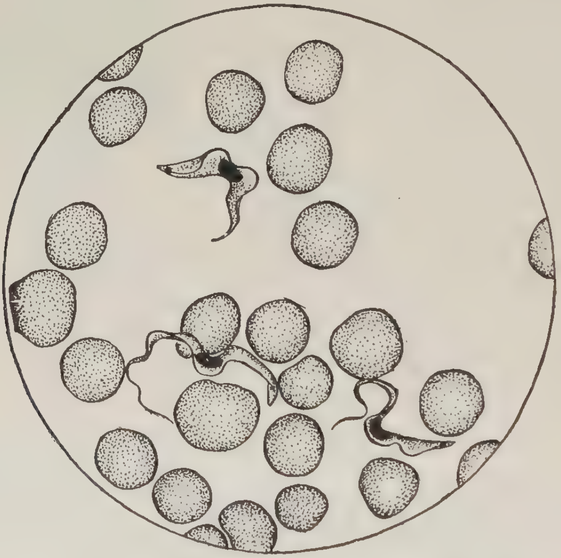

FIG. 45. *Trypanosoma gambiense* in rat blood, showing long, intermediate and short forms all in one microscopic field. × about 1200. Drawn from microphotograph by Minchin.

when they have been ingested by phagocytes. Reproduction takes place by longitudinal splitting of the body; the kinetoplast divides first, next a new flagellum begins to grow out along the margin of the undulating membrane, then the nucleus divides, and finally the body splits from the anterior end backwards (Fig. 46). Crithidial forms are sometimes found in the cerebrospinal fluid.

T. gambiense is readily inoculated into certain kinds of monkeys and less readily into small laboratory animals, unless first passed through a monkey. Various antelopes and other herbivorous animals, and also dogs, can be experimentally infected, and probably occasionally are in nature, but no natural reservoir of this trypanosome among animals has been found except the Situtunga antelope of Uganda, and doubt has been thrown on the correctness of this.

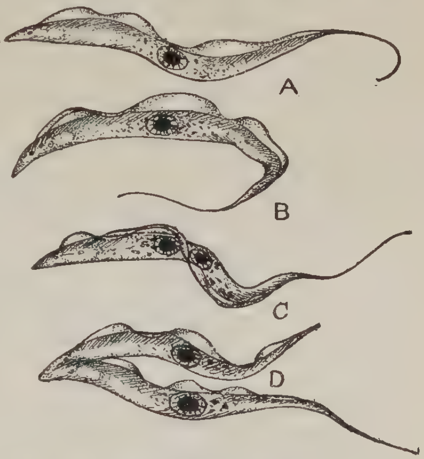

Fig. 46. Method of division in trypanosomes. *A*, elongated form ready for division; *B*, form with divided parabasal body and partially split undulating membrane; *C*, form with double parabasal body, double undulating membrane, and double nucleus; *D*, almost completely divided forms, adhering by posterior ends.

Transmission. — Like others of the polymorphic group, *T. gambiense* is normally transmitted by tsetse flies, but not all tsetse flies serve as intermediate hosts. So far as known at present, *Glossina palpalis* is the chief villain, and the distribution of the infection is practically identical with that of *G. palpalis*, but in some parts of West Africa (northern Nigeria and Cameroons) a smaller species, *G. tachinoides*, also transmits it and seems to be more important than *palpalis*. These species are discussed in Chapter XXVI. Other species can transmit it experimentally but appear not to do so in nature.

There are two methods by which tsetse flies can transmit trypanosomes, — by direct inoculation, or by inoculation after a cycle of development. It was found that the direct transmission could occur up to 48 hours after an infective feed, after which the trypanosomes become so altered that they can no longer cause infection until the cycle of development in the fly has been completed. Probably in nature direct transmission is most common when a partially fed fly finishes its meal on another person. As Duke has shown, when natives push off from the jungly shore of a lake to fish, a swarm of tsetse flies is likely to follow, and if one of these, when biting an infected native, is not allowed to finish its meal in peace, it is likely immediately to try its luck on another individual, injecting trypanosomes which are still in the labial cavity. Duke thinks that particularly virulent strains are built up by such mechanical transfer, and that this process is responsible for severe epidemics, such as that which occurred in Uganda from 1900 to 1910, whereas the "cyclical" transmission keeps up the disease in endemic form. Mechanical transmission is not entirely limited to tsetse flies, but is also possible by stable flies, and even mosquitoes.

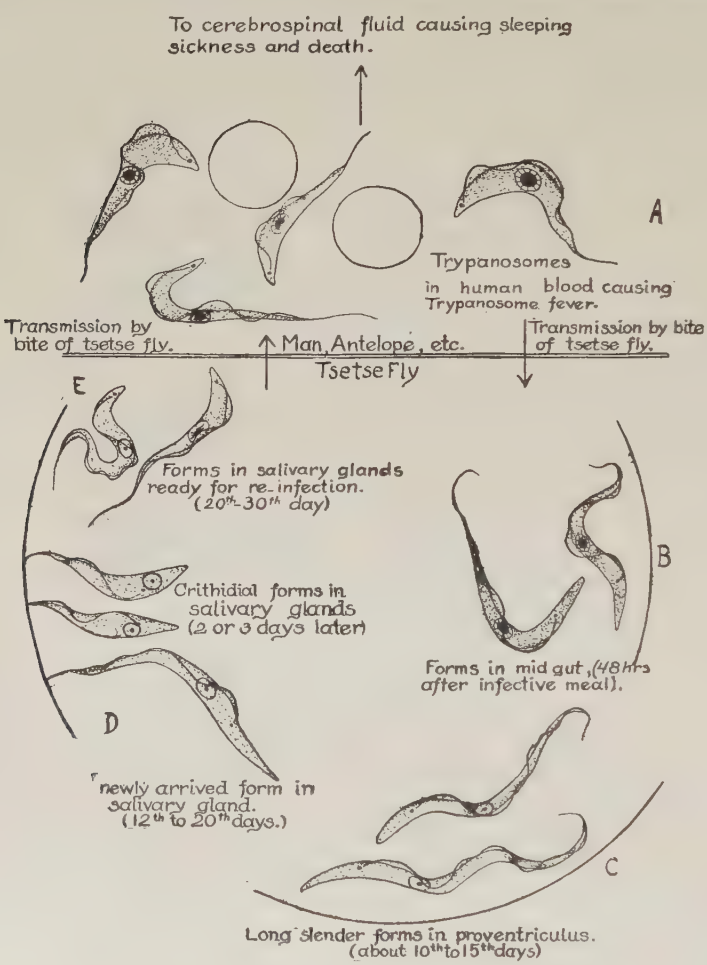
To cerebrospinal fluid causing sleeping sickness and death.
A
Trypanosomes in human blood causing Trypanosome fever.
Transmission by bite of tsetse fly.
Man, Antelope, etc.
Tsetse Fly
Transmission by bite of tsetse fly.
E
Forms in salivary glands ready for re-infection. (20th-30th day)
B
Crithidial forms in salivary glands (2 or 3 days later)
Forms in mid gut, (48 hrs after infective meal).
D
newly arrived form in salivary gland. (12th to 20th days.)
C
Long slender forms in proventriculus. (about 10th to 15th days)

Fig. 47. Life History of *Trypanosoma gambiense*. × 1500. (Constructed from figures by Miss Robertson.)

The "cyclical" transmission is probably more usual. The general nature of the development in tsetse flies was discovered by Bruce and his colleagues in 1911, but the details were worked out by Miss Robertson (1913). According to her observations the critical time for the trypanosomes after they are sucked up by the fly is when the fly feeds the next time, since in many cases they are swept out of the body with the new influx of blood, or digested. Having stood their ground until they have become established in the new influx of blood they multiply so rapidly that permanent infection of the fly is almost çertain. The difficulty experienced by the parasites in establishing themselves in the gut of their insect hosts largely accounts for the relatively low percentage (usually less than 5%) of infections which result from feeding of tsetse flies on infected blood. When conditions are favorable for development in the fly the parasites multiply first in the middle intestine, producing long-snouted forms such as shown in Fig. 47*B*. After the tenth to fifteenth day long slender forms (Fig. 47*C*) are developed, and these move forward in the digestive tract. These slender trypanosomes have long snouts and differ most strikingly from the earlier forms in the appearance of the nucleus (Fig. 47*C*). After several days more the trypanosomes make their way to the fly's salivary glands, to the walls of which they attach themselves by their flagella (Fig. 47*D*) and, rapidly multiplying, undergo a crithidial stage. As multiplication continues free-swimming trypanosome forms are again produced which very closely resemble the parasites in vertebrate blood (Fig. 47*E*) and which are now capable of infecting a vertebrate host. The whole cycle in the fly usually occupies from 20 to 30 days. A temperature between 75° F. and 85° F. is necessary for the full development of the parasite in the fly, ending in invasion of the salivary glands.

The reader will note that no sexual reproduction, such as is so conspicuous in the mosquito cycle of the malarial parasites, has been described in this fly cycle of the trypanosome. It is possible that sexual reproduction of some kind, or at least something which takes the place of it, *does* occur in the tsetse fly, but it has not yet been recognized by scientific observers.

Trypanosoma rhodesiense

The first recorded case of human infection with this parasite was in Rhodesia in 1909. Since then many more cases have occurred, but the infection is limited to an area in East Africa in Rhodesia and Nyasaland, around Lake Nyasa, and neighboring parts of nearby countries. A few outbreaks which might be termed epidemics have occurred, but in general it is remarkably sporadic in its occurrence. The parasite is identical in every respect with *T. brucei* except in its ability to infect man, which the ordinary strains of *T. brucei* apparently do not possess. It is transmitted by *Glossina morsitans,* and in one locality in Tanganyika Territory by *G. swynnertoni.* In animals it behaves exactly like *T. brucei.*

Morphologically this parasite, like other races of *T. brucei,* differs from *T. gambiense* most noticeably in the fact that in small laboratory animals a certain percentage of the trypanosomes have the nucleus displaced backward until it lies in the posterior end of the parasite (Fig. 48).

The occurrence of this new human infection in recent years has led to much interesting speculation. Duke believes that not only are *T. brucei* and *T. rhodesiense* closely related, but that all of the African polymorphic forms are to be interpreted as varieties of one species, differentiated as the result of their environmental experience in both vertebrate and invertebrate host. "These strains," says Duke (1921) "are not immutable but variable, and are determined by the environment in which the species lives; they are not constant under varying external conditions, but each strain is dependent upon, and is produced as a response to, a particular environment." Before the advent of white men and domestic animals in East Africa, *Glossina morsitans* normally fed on the wild game in the drier parts of the country, away from the streams where the natives mainly lived. Under these circumstances there would be little opportunity for a strain capable of infecting man to be developed, as a result, perhaps, of exposure to human blood in the body of the fly, and even if such a strain developed there would be little likelihood of its being transmitted from man to man. But with civilization came destruction of much wild game, a replacement with domestic animals associated with man, and a drawing in of *morsitans* to the vicinity of human settlements to feed on the new hosts, all of which would increase the opportunities for *morsitans* to bite man, with the possibility of developing a strain capable of living in human blood as a consequence. Such a strain, developed under these circumstances,

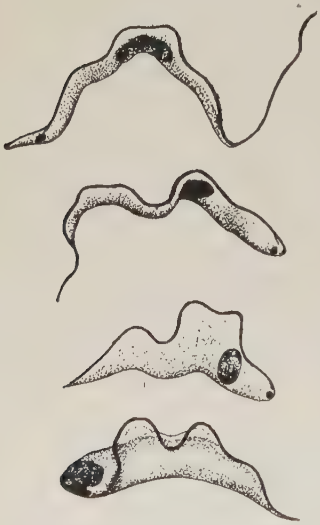

FIG. 48. *Trypanosoma rhodesiense,* from blood of monkey inoculated from case of human sleeping sickness. Note posterior position of nucleus in short blunt forms, especially in lower figure. × 2000. (After Kinghorn and Yorke.)

and perhaps first gaining a foothold in human beings whose powers of resistance were greatly impaired by other diseases, famine, etc., if transferred by direct inoculation in a series of cases, could lead to a highly virulent form, for it is well known that trypanosomes do develop high virulence for a particular animal when transferred directly from individual to individual a number of times, but they are believed to lose any such special virulence, just as they lose tolerance to drugs, when the cyclical development intervenes. Duke suggests that the human infections have come about in such a manner, and result from direct mechanical transmission, and thinks a fly which had a salivary gland infection derived from a human case would not necessarily be capable of causing a human infection. This is at present only speculation, but it seems reasonable. Infectious disease is the result of the interaction of two or more organisms. As surely as there is evolution in the organisms there is evolution in disease. The remarkably sporadic appearance of human cases supports the view that the Rhodesian trypanosome is merely a recurring strain of *T. brucei* which is pathogenic to man, whereas man is highly resistant to ordinary strains of this trypanosome.

Trypanosome Fever and Sleeping Sickness

The course of the disease caused by trypanosome infection is insidious and irregular in the extreme. The Gambian and Rhodesian diseases are essentially alike in their symptoms and in the course they run, except that the latter is usually more rapid in development and more virulent in effect, as a rule causing death within three or four months after infection. The variety of the Gambian disease found in Nigeria is comparatively mild and of long duration.

The bite of an infected tsetse fly is usually followed by itching and irritation near the wound. After a few days fever is felt and a peculiar tenderness of the muscles develops, so that striking against an object causes undue pain. Usually the fever comes and goes at irregular intervals of days or weeks or even months, an infected person sometimes carrying the parasites in his blood, as shown by its infectivity when injected into susceptible animals, for months at a time without any appreciable fever, and in insufficient numbers to be seen readily by microscopic examination. When the attacks of typical trypanosome fever do come they generally are worse in the evening, unlike malarial fevers. After a variable time the victim becomes weak and anemic, probably due to toxins secreted by the parasites, his pulse becomes rapid, and various lymph glands, especially those of the neck, tend to swell up and become tender. Often an irritating rash breaks out on the skin during the early stages of the disease. Loss of ambition and vitality usually figure prominently, and childbirth is seriously interfered with. It is possible that after weeks or months or years of irregular fever and debility the disease may spontaneously disappear, and never become more than trypanosome fever. Usually, however, the parasites ultimately succeed in penetrating to the cerebrospinal fluid of the brain and spinal cord, and " sleeping sickness " results. In some cases the onset of this horrible disease has been known to be delayed for seven years after the beginning of the disease, but usually it comes in the course of a few months. The invasion of the central nervous system is accompanied by a striking accumulation of round cells in and around the walls of vessels in the brain, and by characteristic increases in the cells of the cerebrospinal fluid. Van Hoof and others consider that examination of the cerebrospinal fluid is of great value as an indication of the stage of development of the disease and of the virulence of the trypanosome, and as a gauge of success of treatment and probable outlook for the patient.

Sleeping sickness is ushered in by an increase in the general physical and mental depression, the symptoms being not unlike those of hookworm disease but more pronounced. The victim wants to sleep constantly and lies in a stupor; his mind works very slowly, and even the slightest physical exertion is obnoxious. Eventually the sleepiness gets such a hold on him that he is likely to lose consciousness at any time and even neglects to swallow his food. After weeks of this increasing drowsiness, his body becomes emaciated, a trembling of the hands and other parts of the body develops, with occasional muscular convulsions and sometimes maniacal attacks. He finally passes into a state of total loss of consciousness ending in death, or death may end the unhappy condition earlier during an unusually intense convulsion or fever, or through the agency of some complicating disease. If untreated, death is the inevitable outcome. A large per cent of infections occur among people of middle age. Old people are significantly few in number in sleeping sickness districts. The presence of these few may be due to a natural or acquired immunity. In Nigeria the disease predominates in young people, possibly because they are water-carriers and are therefore more exposed to the bites of tsetse flies.

Treatment. — There has been a vast amount of experimental and practical work done on the treatment of trypanosome infections, as the result of which the disease is not the hopeless thing it once was. It is doubtful if cure can yet be effected after the disease has reached the sleeping sickness stage, but in earlier stages it can be controlled, often apparently cured, by prolonged courses of injections, and the death rate of infected people has been markedly reduced by systematic treatment. The effective drugs are mainly arsenic compounds, such as the arsphenamins, atoxyl, tryparsamide, etc., and antimony compounds, such as those used in leishmaniasis. Another drug, "Bayer 205," has also been used with much success. The Rhodesian trypanosome is much more resistant to all of these drugs than is the Gambian one, and infections with it are seldom amenable to treatment unless taken in hand very early.

Alternate doses of arsenic and antimony drugs give the most reliable results, for the trypanosomes tend to build up a tolerance for them, much as a man may build up a tolerance for arsenic or other drugs. This tolerance is retained through repeated passages in animals, and gives rise to "arsenic-fast" or "antimony-fast" strains of trypanosomes. Gonder believed that *T. lewisi* of rats lost its drug tolerance when passed through the intermediate host, a flea, the insect cycle thus eliminating at a stroke an acquired character which had been maintained through thousands of generations in passages from rat to rat. If this is confirmed, and universally true, it would mean that permanent drug-fast strains of human trypanosomes would be unlikely to be established in nature. Duke (1927), however, thinks he has evidence that *T. brucei* does not lose its tolerance after going through its cycle in a tsetse fly. This matter is an important one, for it involves also the question of the power of trypanosomes to retain exalted virulence for particular animals after the fly cycle, a matter which may mean much in the case of *T. rhodesiense*.

Although the use of immune serum from animals which have recovered has been very successful in curing and immunizing various lower animals against trypanosome infections, there has so far been no successful application of the method to the treatment of human infections.

Prevention. — The ultimate control of sleeping sickness resolves itself into the question of controlling or locally exterminating the particular tsetse flies which serve as intermediate hosts. This is discussed in detail on pp. 542–544.

In the meantime other methods for controlling, if not entirely eliminating, the disease have been utilized with more or less success. These consist in reducing, as far as possible, contacts between tsetse flies and man, by the careful selection of sites for camps and villages, local clearing of brush from river edges, etc. Extension of sleeping sickness areas can be controlled to some extent by control of the movements of natives in infected areas. In the Great Lakes region of Africa attempts have been made to eliminate the disease from certain shores and islands, where it was very prevalent among the fishing population, by a wholesale depopulation and removal from the shores, in the hope that the tsetse flies would lose their *T. gambiense* infections, so that when the uninfected inhabitants returned they would be in no further danger. The difficulties in accomplishing this were very great, and the depopulation was not as complete as was thought, so the method did not prove a complete success.

Another valuable control measure is the sterilization of the peripheral blood of all infected individuals by injections of arsenical drugs, a method resulting from the work of Van den Branden, who found that even a single injection of these drugs would render the blood trypanosome-free for many months. In some places in West Africa the incidence of sleeping sickness has been very appreciably reduced by giving courses of injections, usually six at intervals of a week, the blood then remaining free of parasites for about 18 months. The success of these methods is evidence in itself that there is no important reservoir of infection other than man himself. Another method of protection advocated by the French is an " animal screen " of pigs or other animals to detract the flies from man, a method diametrically opposite to that advocated by some investigators, namely a wholesale destruction of game animals which serve as natural hosts of the flies. The question as to whether game should be destroyed with the hope that tsetses would disappear with them, or be encouraged, and even farmed, to serve as buffers between man and fly, is still a matter on which experts with long experience disagree. The matter is discussed further in the section on tsetse flies

Chagas' Disease

A different type of human trypanosome infection was found by Chagas, in 1909, in the State of Minas Geraës in Brazil. He discovered that the houses of the natives were infested with large blood-sucking bugs, *Triatoma megista*, which the natives called barbeiros, and that these bugs were infected with flagellates which, when inoculated into monkeys and guinea pigs, caused acute infections. On further investigation he found that in the infested houses there were frequent cases, especially among infants and young children, of an acute disease characterized by fever, enlarged glands, anemia, and disturbances of the nervous system. In one of these cases trypanosomes were found in the blood, and in others they were demonstrated by injection of animals. These trypanosomes, named *T. cruzi*, have been the subject of a large amount of experimental work since Chagas first discovered them.

The Parasite. — *Trypanosoma cruzi* is a curved, stumpy trypanosome about 20 μ long, with a pointed posterior end, an elongated nucleus in the center of the body, a large egg-shaped kinetoplast close to the posterior end, a narrow and only slightly rippled undulating membrane, and a moderately long free flagellum (Fig. 49). Some narrow and some broad individuals are found, which Chagas thought might be male and female forms, but this is very unlikely, and it is probable that they are merely young and mature individuals.

Unlike other trypanosomes this species as found in the blood never exhibits stages in division, and this fact led Chagas to search for some other form of multiplication. He found in the lungs of infected animals what he thought to be a process of division of the trypanosomes into eight parts, but this later was found to be a stage in the life history of an entirely different parasite. The real method of multiplication was first discovered by Vianna in the bodies of man and animals who had died of the disease. Vianna found in various tissues, especially in the walls of the heart, the striped muscles, the central nervous system and various glands, greatly swollen cells which served as cysts, enclosing a mass of rapidly dividing trypanosomes, varying in number from just a few to many hundreds. In younger cysts the parasites are round in form and exactly resemble Leishman bodies (Fig. 50*A*), while in older cysts the flagellum can be seen on many individuals and the trypanosome form becomes evident (Fig. 50*B*). When the enclosing cell has swollen to the bursting point, the swarming mass of trypanosomes is liberated. Each parasite, unless destroyed, then penetrates a new cell somewhere in the body, usually near where it originated, rounds up into a Leishmania form, and begins the process of reproduction again. Only in the early acute stage of the disease can the parasites live in the blood, since the blood serum rapidly reacts by the formation of antibodies, and becomes injurious to the trypanosomes. Chagas believed that the parasites could live within the corpuscles as well as in the serum, but later work does not confirm this. The parasites are very scanty in the blood of chronic cases of the disease, so that often they can only be discovered by inoculation of animals or cultures, even though their cysts may be abundant in various tissues and glands in the body.

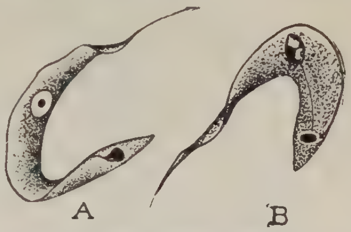

FIG. 49. *Trypanosoma cruzi* in blood of experimentally infected monkey. *A*, so-called male form; *B*, so-called female form. (After Chagas.)

T. cruzi is a very versatile trypanosome. Its natural hosts appear to be armadillos, especially *Tatusia novemcincta*, opossums, and rodents, but it can thrive in the blood of monkeys, marmosets, guinea pigs, rats, rabbits, cats, dogs, and other animals. Man seems to be more resistant than the majority of these.

Intermediate Hosts, and Transmission. — The insect which transmits *T. cruzi* to man in Brazil is a large black and red bug, *Triatoma megista*, known to the natives as the " barbeiro." It is a Reduviid, and nearly related to the cone-nose or " Mexican bedbug " of our Southern States; it is a fierce, blood-sucking insect which infests the dirty thatched or mud houses of the natives, coming out at night, and skillfully secreting itself in the daytime (see p. 452, and Fig. 213). In Venezuela another bug of the same family, *Rhodnius prolixus*, but garbed in brown and yellow, assumes the rôle of transmitter to man (see p. 453). This bug, called the " pito," has habits almost exactly like those of the barbeiro. Many other species of blood-sucking Reduviids have been found to serve equally well as intermediate hosts, and as transmitters to natural or experimental animals. But this is not all, — *T. cruzi* is nearly as versatile with respect to its intermediate host as to its vertebrate host, which is much more unusual. In addition to probably all kinds of blood-sucking Reduviids, bedbugs and even ticks serve as satisfactory intermediate hosts. Mayer (1919) found a tick (*Ornithodoros moubata*) still infected at the end of five years! It is discomforting to have such an adaptable parasite capable of causing human disease, but fortunately man is one of the least susceptible hosts.

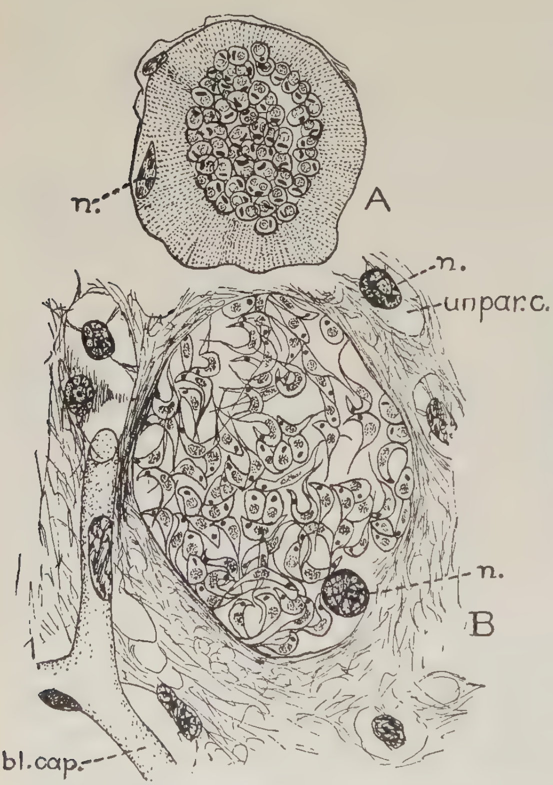

FIG. 50. *Trypanosoma cruzi*. *A*, cyst containing *Leishmania* forms in muscle fiber of guinea-pig, cross section; *n.*, nucleus of muscle fiber. *B*, older cyst, containing trypanosome forms, in neuroglia cell in gray matter of cerebrum; *n.*, nucleus of parasitized cell; *bl. cap.*, blood capillary; *unpar. c.*, unparasitized cell. × 1000. (After Vianna.)

The cycle of development of *T. cruzi* in the intermediate host is not as thoroughly understood as in the case of some trypanosomes. According to Chagas a cycle of development as shown in Fig. 51 takes place; he suggests that the crithidial forms play no part in transmission, and merely represent a return to a primitive condition suitable for survival in bugs, and for transfer from bug to bug, whereas the trypanosome forms later produced (as the result of sexual reproduction, according to Chagas) are the infective forms, and that these invade the body cavity and the salivary glands. If this invasion ever occurs it must be rare, and probably is an error. According to Brumpt the ingested trypanosomes quickly change into stumpy crithidial forms which multiply rapidly, often producing Leishmania forms; the daughters later change into a longer crithidial type and accumulate in the posterior part of the mid-gut. About 8 to 10 days or more after infection, small trypanosome forms appear and pass backward into the rectum, whence they are voided with the feces. These forms are infective for animals when inoculated, and are undoubtedly the means of spreading the disease, by contaminating the wounds made by the bugs. The infection can also spread from bug to bug either by cannibalism or by ingestion of liquid feces. This is discussed further on p. 455. Once a bug becomes infective

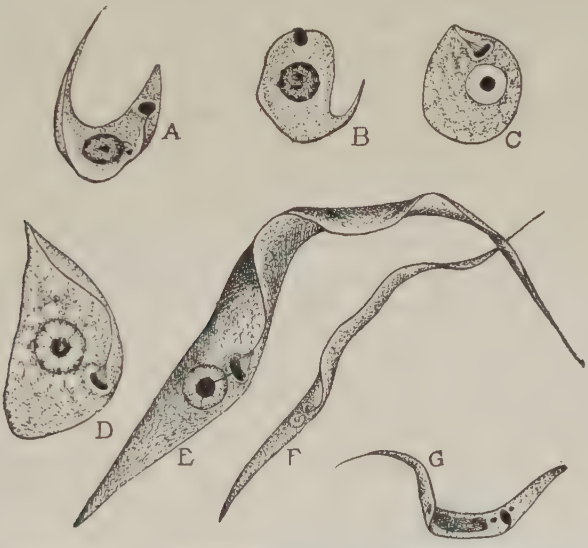

Fig. 51. Development of *Trypanosoma cruzi* in digestive tract of bug (*Triatoma megista*). *A*, freshly ingested form; *B*, rounding up and loss of flagellum, 6 to 10 hrs. after ingestion; *C*, *Leishmania*-like form in mid-gut, 10 to 20 hrs. after ingestion; *D*, redevelopment of flagellum and undulating membrane, 21 hrs. after ingestion; *E* and *F*, crithidial forms in hind-gut, 25 hrs. after ingestion; *G*, trypanosome form from salivary gland, 8 days or more after ingestion. (After Chagas.)

it remains infective for a year or more, very likely for the rest of its life.

Human Infection. — The distribution of human trypanosomiasis as compared with the distribution of Reduviids which harbor trypanosomes that are closely related to, if not identical with, *T. cruzi* seems to the writer to be of great biological interest. All the way from the Pampas of Argentina through the forests of tropical America to the deserts of Arizona, species of *Triatoma* and *Rhodnius* harbor *cruzi*-like trypanosomes, and these trypanosomes are transmitted in nature to such animals as armadillos, opossums and rodents on which the bugs habitually feed. Nearly all of these bugs occasionally vary their diet by biting human beings, but only two of them, *Triatoma megista* and *Rhodnius prolixus*, and to a considerably smaller extent *Triatoma infestans*, habitually live in human habitations and subsist primarily on human blood. Now it is quite likely that *T. cruzi* was originally a parasite of the bugs alone, but that with the development of blood-sucking habits on the part of their hosts they became adapted to living in the presence of blood of the species of vertebrates on which the bugs habitually fed. It is easy to understand that a flagellate which was deluged with armadillo blood, for example, every time its hosts indulged in a meal, if subsequently inoculated into an armadillo, might be able to survive in the blood and tissues of that animal, and cause infection in it. Once thoroughly adapted to life in one vertebrate, it could also succeed in establishing itself in many others. Thus infected armadillo blood inoculated into dogs, rodents or monkeys causes infection in these animals.

Man, however, is evidently very highly resistant to the trypanosome, and it seems possible that both trypanosome and human being have to be especially prepared for each other before they can live together in the relation of parasite and host. The trypanosome may have to go through a course of training by exposure to human blood in the gut of its insect host before it can have a reasonable chance to survive when inoculated into human beings. It seems significant that human infections occur only in those places where infected bugs feed *habitually* on human beings. But even in the case of trypanosomes thus adapted, infection apparently does not succeed unless the defenses of the human host are weakened. In Brazil *T. cruzi* infections in man are common only in a goiterous district in Minas Geraës, and occur mainly in children and infants; a few cases have been recorded from São Paulo. In Argentina a few scattered cases have been recorded, also in a goiterous district; in Venezuela the recorded cases have also occurred in a region of endemic goiter. The single known case from Peru occurred in an individual who is described as having suffered long from forest fevers.

When Chagas first discovered human trypanosome infections in the regions of endemic goiter in Minas Geraës, he believed that the goiter, with all its sinister consequences, — myxedema, infantilism, cretinism, etc., — were caused by the trypanosome infection, through a supposed toxic effect on the thyroid gland. However, no such effect is produced in animals, and Kraus, Niño and others have found areas of endemic goiter in northern Argentina where trypanosome infections are absent in the bugs as well as in human beings, and other areas where there was no goiter but where a high percentage of bugs were infected. Animals in which the thyroid gland is removed or partly removed are much more susceptible to all sorts of infections than are normal animals; in fact, removal of the thyroid is one of the methods commonly adopted for making animals more susceptible to such diseases as kala-azar, leprosy, etc. It seems to the writer, therefore, that Chagas got the cart before the horse, and that it is much more likely that people get *T. cruzi* infections because they have goiter, than vice versa.

It has been demonstrated that in dogs the disease can be transmitted from mother to offspring before birth. It is possible that prenatal infection may also occur in the case of man, since many cases have been observed in very young babies.

The Disease. — Acute cases of Chagas' disease are especially common in infants or young children, and occur almost exclusively in regions of endemic goiter, the latter being thought by Chagas to be a manifestation of a chronic infection (see above). In acute cases the parasites are usually fairly numerous in the blood, but later they become very scanty and can only be found by injection of large amounts of blood into animals. The disease is usually marked by a high and continuous fever which lasts for several weeks, often without remission; by enlargement of the lymph glands, and also of the spleen and liver; by a progressive anemia which may become very profound; and by nervous disturbances, such as delirium, convulsions, extreme lassitude, or paralysis. Very commonly there is a marked edema, especially of the face, so that the skin has a peculiar feeling of "crepitation." This symptom, however, may be connected with the goiter rather than the trypanosome infection. In severe cases death may occur in two or three weeks, but many cases appear to suffer very little, and they either recover or go into a chronic state. The parasites have been observed to be temporarily present in the blood of individuals with malaria or other diseases without producing any symptoms directly referable to them. Chagas believes the chronic cases are very common, but the evidence for the presence of trypanosome infections in many of the cases which he considers chronic trypanosomiasis has not been brought forth. In animals the trypanosomes tend to localize in particular organs, especially the heart, lymph glands or central nervous system, and they produce symptoms according to where they localize. Disturbance of the function of the heart is very common, and according Chagas is the commonest chronic manifestation in man, but while trypanosomes multiplying in the heart muscles have been demonstrated in a few autopsies, in the majority of the cases of heart disturbances which have been attributed to trypanosomiasis there has been no evidence whatever of the presence of trypanosomes. Villela obtained a " neurotropic " strain of the parasite by inoculation of a dog from an infected armadillo; this trypanosome had a special predilection for the nervous system, and regularly caused a variety of nervous symptoms such as convulsions, paralysis, etc. Similar motor disturbances have been observed in human cases.

Treatment and Prevention. — There seems to have been very little work done on the treatment of Chagas' disease, but it is probable that the drugs which are effective against other trypanosomes may also have some value against this, although it may be expected that treatment will be far more difficult in the case of a parasite which lives most of its life intra-cellularly, than of one which lives between the cells, even if in the tissues. It is interesting to note that the discovery of the value of tartar emetic against leishmaniasis was the outcome of work by Vianna on *T. cruzi* infections.

Prevention of the disease consists largely in avoiding and exterminating the house-dwelling Reduviids. It is practically impossible to keep the bugs out of mud or thatched houses. For this reason the rebuilding of houses with other material is being urged everywhere in Brazil, and with good results. The town of Bello Herizonte, for example, which was formerly termed " a nest of cretins " is said to have been nearly freed from Chagas' disease, due to remodeling of the houses. If this means that endemic goiter is disappearing merely as the result of eliminating bugs infected with *T. cruzi*, further investigation of the relation between goiter and trypanosomiasis is required. It is possible, however, that the water supply or other factors were improved as well as the construction of the houses.

Since it now seems possible that human infection results only from infection with trypanosomes already adapted to human blood, and from inoculation of individuals whose resistance is markedly lowered, it is doubtful if much would be gained by a campaign against armadillos and other reservoir hosts. The gradual elimination of bugs from human habitations, and the protection of sick individuals from their bites by screening at night, are the measures which are suggested by the known facts.

CHAPTER IX

MALARIA

Importance. — It was pointed out in Chapter III that man is peculiarly exempt from attack by all but a few of the Sporozoa, but that among these few were the parasites of malaria. Of all human diseases there is none which is of more importance in the world today than malaria, and this in spite of the fact that we have a very full knowledge of its cause, the manner of its spread, its cure, and means of prevention. It has been estimated to be the direct or indirect cause of over one-half the entire mortality of the human race. Sir Ronald Ross says that in India alone it is officially estimated that malaria kills over one million persons a year, a greater number of deaths than was caused by the great European war in the first two years of its existence. When there is added to this the thousands from the rest of Asia, Africa, Southern Europe, South and Central America, and the southern part of our own country who are annually sacrificed on the altar of the malarial parasite; the millions of others who are broken in health, incapacitated for work and made easy victims of other diseases; the valleys, countries, and even continents which have been barred from full civilization and development by this more than by any other cause; then only can we get a glimpse of the real meaning of malaria to man. Ross argues convincingly that the downfall of the great Greek empire and the present poverty-stricken, blighted condition of many parts of Greece is probably due primarily to the invasion of that country, not by burning and devastating armies of men, but by the malaria parasite, an infinitely more terrible though unseen foe which destroyed the new-born infants, undermined the health of the children or killed them outright, rendered the richest agricultural lands uninhabitable, and, in a word, sapped the vitality of the people until the boasted power and glory of Greece is but a mocking memory.

Though historians and economists have failed to recognize it, the rôle of malaria and other endemic diseases must have played an enormous part in the history of the world and in the progress of nations. Malaria and its powerful accomplice, the hookworm, are largely responsible for the present deplorable condition of some parts of our own South. Dr. Howard estimated in 1907 that there were nearly 12,000 deaths a year in the United States from malaria. This, however, is probably almost inconsiderable when the amount of damaged health and weakened resistance to other diseases is taken into consideration. Dr. Von Ezdorf, of the U. S. Public Health Service, in an attempt in 1914 to estimate the prevalence of malaria in the United States, obtained data, based on morbidity reports, which indicate that at least 4% of the population of eight southeastern states — 600,000 people — are affected by the disease annually, and found by 13,526 blood examinations that over 13% harbored malarial parasites in their blood, the percentage being much higher in negroes than in whites. Dr. Howard thinks that an estimate of 3,000,000 cases of malaria a year in the United States would not be too high. Millions of acres of fertile land in this country are rendered useless or only imperfectly cultivable. It has been stated (Fricks, 1920) that malaria, through sickness and decreased efficiency, causes a greater economic loss to the malarious sections of the South than all the other preventable diseases combined — approximately a billion dollars a year. This is the condition in the United States, a large portion of which is relatively free from malaria, and in no part of which is the disease so prevalent or so destructive as in the tropical portions of Asia, Africa and South and Central America. In a broad way one-third of the population of highly malarial countries suffer from the disease annually. Obviously the importance of this disease to mankind is not likely to be overestimated.

History. — " Malaria " means bad air, and was therefore applied to a number of fevers which were commonly associated with the bad air of swampy regions. The idea that malaria is caused by bad air, unwholesome odors, damp night winds, or impure drinking water is even yet adhered to not only by some of the populace but even by a few unenlightened medical men. Ross says that it takes ten years for the world to grasp a new idea, but his estimate is far too low. It was in 1880 that Laveran, a French army surgeon in Algeria, discovered a parasitic organism which he proved to be the true cause of malarial fevers. Dr. King, of Washington, in 1883 suggested the probability of malaria parasites being spread by mosquitoes, adducing much circumstantial evidence in support of his views. It was not until 1898, however, that Sir Ronald Ross, of the Indian Medical Service, experimentally proved that malaria parasites are absolutely dependent upon certain species of mosquitoes for their transmission, and worked out the details of the transmission in the case of bird malaria. Immediately afterwards Grassi and his pupils worked out the cycle of human malaria in Anopheles. In 1911 the parasites of malaria were first successfully cultured outside the human body by Bass and Johns at New Orleans, which has led to new and valuable discoveries. Other workers deserve no less credit, perhaps, for suggestive ideas, or for additional facts concerning the life and control of the malarial parasites. The ultimate results of their discoveries have only begun to be felt, but already such enterprises as the building of the Panama Canal have been rendered possible, and the conquest of the tropics is rapidly becoming a fact.

Malaria Parasites. — The malaria parasites belong to the class Sporozoa, or " spore animals," which, as we have seen in Chapter III, are characterized especially by their life cycles, which involve two phases of development, one asexual and one sexual. There are two subclasses of Sporozoa, including respectively the Gregarines, in which the two uniting sex cells are alike in size, and in most of which there is no asexual multiplication, and the coccidia-like forms, to which the malaria parasites belong, in which the sex cells are much like eggs and sperms, and in which the asexual forms multiply by schizogony (see p. 36). Further division of the Sporozoa into orders and suborders is based mainly on differences in details of the nature, formation, or behavior of the sex cells and of the resulting zygote, which we need not discuss here. The malaria parasites belong to the suborder Hæmosporidia, which includes blood-inhabiting protozoa of mammals, birds and reptiles.

The true malaria parasites, which constitute the genus *Plasmodium*, undergo both schizogony and gametocyte formation in the red blood corpuscles, while the other two genera of Hæmosporidia, *Hæmoproteus* and *Leucocytozoön*, undergo schizogony in endothelial cells, and appear in the blood stream only as gametocytes.

Three species of *Plasmodium* are universally recognized as causing malaria in man, but whether there are others is still a question about which there is much dispute. The commonest and most widely distributed species is *Plasmodium vivax*, which causes " benign tertian " or merely " tertian " malaria. It is essentially the parasite of relapsing and chronic malaria. Of somewhat more limited geographic distribution, being largely confined to the tropics and sub-tropics, is *P. falciparum*, the cause of " æstivo-autumnal," " malignant tertian," or " subtertian " malaria. It is a particularly deadly species, and the disease it produces is likely to appear in epidemics. Fortunately it is less resistant to quinine than is *P. vivax*. The third species, *P. malariæ*, causing quartan malaria, is relatively uncommon, though more frequent in temperate than in tropical countries. It is said to be more resistant to treatment than either of the others.

Life History of *Plasmodium falciparum*; Human Cycle. — The life history of malarial parasites may well be exemplified by that of the malignant æstivo-autumnal parasite, *Plasmodium falciparum*, as diagrammatically shown in Fig. 52. When first injected into human blood by a mosquito the animal is exceedingly minute (Fig. 52*A*). It immediately enters or attaches itself to a red blood corpuscle, where it grows until it occupies one-half or two-thirds of the corpuscle, meanwhile undergoing a number of different forms. It first goes through a " signet ring " stage (Fig. 52*B*), the ringlike appearance being due to the presence of a transparent area occupying the middle of the parasite, while the tiny round nucleus occupies a position at one side of the parasite, simulating the setting in a ring. As the parasite grows larger it becomes irregular in shape (Fig. 52*C*) but, unlike *P. vivax*, it does not become strikingly active; instead of sprawling itself all over the cell, it remains a fairly compact body. Although it has been taken for granted that malarial parasites penetrate the blood corpuscles and live inside of them investigations by Lawson (1913–1919) and Sinton (1922) suggested that this might not be the case at all, but that the parasites may attach themselves to the surface of the corpuscles, squeezing up little mounds of the substance of the corpuscles and encircling these mounds with their bodies, just as a bit of skin might be squeezed up between the fingers. They are even suggested as wandering from corpuscle to corpuscle in search of hemoglobin, like bees searching honey in flowers. A number of facts give support to this theory: it affords a logical explanation for the ring forms of the parasite; it explains the occasional distinct projection of the parasites at the periphery or edge of the corpuscles; and it accounts for the ease with which the parasites may be distorted in making blood smears. Another argument in favor of this theory as opposed to the intracorpuscular theory is that the hemoglobin in the corpuscles is believed to be in a more or less solid state, and would therefore make it difficult for the parasites, if situated inside, to indulge in such active movements as they do. On the other hand, Ratcliffe (1928) cut sections of parasitized corpuscles in which the parasites certainly appear to be intracellular. It is, therefore, still undetermined whether the parasites live in or on the corpuscles.

As the growing schizont develops there is a distinct tendency for the affected corpuscles to clump together and to adhere to the walls of the vessels, thus clogging the tiny capillaries. In this way the capillaries of such organ as brain, spleen, bone marrow and others may be obstructed to a fatal degree. Three-fourths of the life cycle of the parasites is usually passed in the plugged capillaries so that only during one-fourth of their cycle can they be found readily in the circulating blood. During the course of development blackish pigment granules of melanin, resulting from the decomposition of hemoglobin by the parasite, is formed.

After about 40 hours the nucleus of the schizont begins to undergo repeated division until there are from 10 to 15, or even as many as 32,

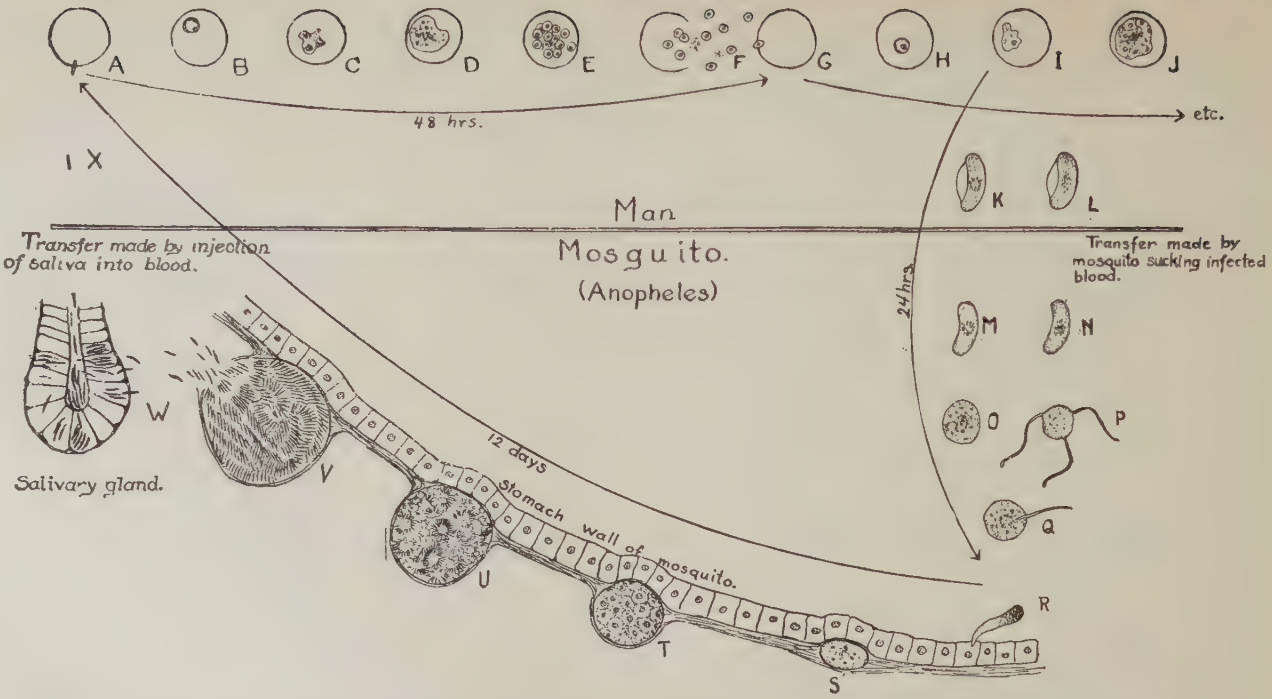
A
B
C
D
E
F
G
H
I
J
48 hrs.
etc.
X
K
L
Man
Mosquito.
(Anopheles)
Transfer made by injection of saliva into blood.
Transfer made by mosquito sucking infected blood.
24 hrs.
M
N
O
P
Q
R
W
Salivary gland.
V
12 days
Stomach wall of mosquito.
U
T
S

FIG. 52. Life history of malaria parasite (*Plasmodium falciparum*); *A*, spore from salivary gland of mosquito entering red blood corpuscle; *B*, young "ring" stage; *C*, later ameboid stage; *D*, adult parasite ready to sporulate; *E*, young parasites in corpuscle, resulting from sporulation (note residual pigment granules); *F*, *G*, liberation of young parasites and attack of new corpuscle; *H*, *I*, and *J*, repetition of growth, sporulation, etc.; *K* and *L*, female and male cells (gametocytes), respectively, in blood stream; *M* and *N*, same, in stomach of mosquito, remnants of blood corpuscles digested off; *O*, mature female gamete; *P*, formation of "flagellated body," *i.e.*, extrusion of male gametes from male gametocyte; *Q*, fertilization; *R*, young wormlike body, developed from fertilized egg, penetrating wall of mosquito's stomach; *S*, *T* and *U*, stages in development of spore filled capsule on outer wall of mosquito's stomach; *V*, mature capsule bursted, liberating spores into body cavity; *W*, penetrating of spores into salivary glands; *X*, injection of spore into human blood. *A–Q*, × 1000, *R–X*, × 500. (Suggestions from various authors.)

small nuclei. The cytoplasm forms small buds around the nuclei, which finally separate to form a little cluster of independent cells, the merozoites (Fig. 52*E*). The pigment granules are left in one or more little masses with the residual cytoplasm not used in the formation of the merozoites. By this time the parasitized corpuscle is little more than a shell. The parent cell now bursts and liberates the daughters (Fig. 52*F*), which attack neighboring corpuscles and begin the cycle of development over again. The pigment and other waste products which are left behind when the parasite multiplies are released into the blood stream where they are carried to all parts of the body and deposited in the spleen or other organs or under the skin, causing the sallow color so characteristic of malarial patients. It is at the time of the bursting of the corpuscles and release of the waste matters that the characteristic chills and fever of malaria are felt. Since the cycle from one generation to the next is usually about 48 hours in the æstivo-autumnal parasite the attacks of ague are felt at these intervals. In this malignant type of malaria the bursting of all the parasitized corpuscles and release of waste matter does not occur so nearly simultaneously as it does in the other species, the result being that the paroxysms of chill and fever are drawn out over many hours.

A "quotidian" type of malignant malarial fever in which agues occur every 24 hours is occasionally met with, the parasites of which are thought by some authors to constitute one, or even two, distinct species. The majority of cases of malaria with daily-recurring fevers are due to double or triple infections, the different broods maturing on different days.

This rapid process of multiplication in the human blood results in a short time in an enormous number of parasites, sometimes many billions. The actual quantity of parasites in a human body in a case of severe æstivo-autumnal malaria has been estimated at 600 cc., or over one pint. It may or may not mean more to the reader to know that such a quantity of malarial parasites would number 3,000,000,000,000. A better conception of the real meaning of such a number may perhaps be gained when it is realized that to count off this number at the rate of 100 per minute day and night without cessation would require 30 times the period of time that has elapsed since the birth of Christ. Eventually, however, either the parasite kills its host, which very commonly happens with this particular species, or the host, by the development of a temporary immunity in his body, kills or, as it more often happens, suppresses the parasite. Such a course of events, unaltered, would lead to a very early and complete extermination of the parasite. There is a second chapter in the life history of *Plasmodium* which saves it from such an early death.

After the parasites have been developing in the blood for a while there are developed special sexual forms or gametocytes, male and female, in the form of sausage-shaped crescents (Fig. 52*K* and *L*). The crescents may persist in the blood for several weeks, gradually disappearing after all other symptoms of infection have vanished. Only slight differences can be seen between the male and female gametocytes; the female stains a deeper blue than the male, the nucleus is smaller and stains a deeper red, and the pigment granules are more closely concentrated around the nucleus (Fig. 52*K* and *L*).

Mosquito Cycle. — When sucked into the digestive tract of the mosquito these gametocytes begin a complex developmental cycle, providing conditions of temperature are favorable. The *most* favorable temperatures are between 75° and 85° F. The digestive fluids dissolve the remnant of the blood corpuscles, but the crescents resist digestion (Fig. 52*M* and *N*) and become more obviously sexually differentiated. The female gametocyte develops into an inactive spherical macrogamete (Fig. 52*O*), the nucleus of which moves towards the surface. In the male gametocyte, on the other hand, the nucleus divides into a number of particles, and long thin processes of cytoplasm project from the surface, each invaded by a chromatin particle. Thus the gametocyte appears to have from 4 to 8 lashing, flagellum-like structures attached to it (Fig. 52*P*), whence it became known as the " flagellated body." These flagellum-like structures are in fact the microgametes, which correspond to the sperms of higher animals. They break loose and swim actively about among the corpuscles ingested by the mosquito, in search of a macrogamete. Having found one, a single microgamete enters the side where the nucleus is (Fig. 52*Q*) and a fusion occurs, just as when an egg cell is fertilized by a sperm.

The result of the union of the filament from the flagellated body with the inactive female gamete is a " zygote," which corresponds in every way to a fertilized egg of a higher animal. This new individual, the beginning of a new generation, grows, elongates, and becomes quite like a little worm (Fig. 52*R*); it is 18 to 24 μ in length and 3 to 5 μ in width, and is called a vermicule or oökinete. It now wriggles and worms itself about in the stomach of the mosquito and penetrates the wall, lodging itself between the inner and outer linings of the stomach (Fig. 52*S*). Here more rapid growth takes place and a capsule or cyst wall develops, formed partly by the parasite, and partly by the elastic membrane lining the mosquito's stomach. The cyst protrudes like a little wart on the outer surface of the stomach wall (Fig. 53). The cyst grows until it has a diameter of 50 to 60 μ. Meanwhile the contents of the capsule undergo important changes. The nucleus divides repeatedly until an enormous number are present, and at the same time vacuoles appear in the cytoplasm which run together and convert the cytoplasm into a sponge-like mesh, all over the surfaces of which the minute nuclei arrange themselves, and slender spindle-shaped bodies, the sporozoites, develop from them, projecting like the "stickers" on a chestnut bur. Eventually the numerous slender sporozoites, each about 15 μ in length, break loose from their moorings and form a tangled mass in the capsule, which is crammed with them to the bursting point (Fig. 52*V*). Such a capsule may contain over 10,000 spores, and there may be as many as 500 capsules on a single mosquito's stomach (Fig. 54). About 12 days or more, according to temperature, after the infected blood was swallowed by the mosquito, the capsule becomes mature and bursts, releasing the spores into the body cavity of the mosquito. From here the little parasites make their way to the three-lobed salivary gland (Fig. 54, *sal. gl.*) lying in the fore part of the thorax and connecting with the sucking beak. They assemble in the cells lining the salivary glands (Fig. 52*W*) and remain there perhaps for weeks, until the mosquito bites. When this happens the parasites flow with the poisonous saliva into the puncture made by the mosquito and, should the prey of the mosquito be a human being, the whole process of asexual multiplication in the human blood corpuscles begins over again. Since it takes 10 or 12 days for the sexual cycle to be completed in the

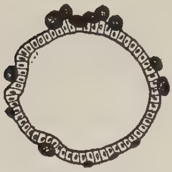

FIG. 53. Cross section of stomach of *Anopheles* showing capsules (oöcysts) of subtertian malaria. × about 30. (After Grassi.)

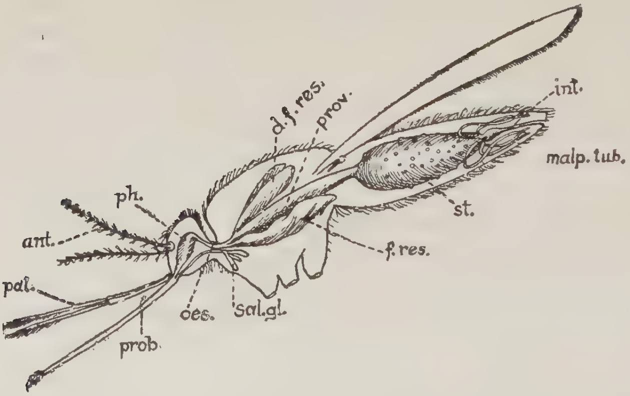

FIG. 54. View of digestive tract of *Anopheles*, showing spore-filled capsules of malaria parasites on wall of stomach; *pal.*, palpi; *prob.*, proboscis; *ant.*, antennæ; *ph.*, pharynx; *œs.*, esophagus; *sal. gl.*, salivary glands; *f. res.*, ventral food reservoir; *d. f. res.*, dorsal food reservoirs; *prov.*, proventriculus; *st.*, stomach; *malp. tub.*, malpighian tubules; *int.*, intestine. × 10.

case of æstivo-autumnal malaria, an infected mosquito is not dangerous for at least this length of time after biting a malarial patient. However, once the new generation of spores has been developed, the mosquito remains dangerous for several weeks and may infect many persons, as not all the parasites are poured out of the salivary glands at one biting.

Other Species. — The other species of malarial parasites differ only in minor details of their structure and development. The tertian parasite, *Plasmodium vivax*, during the early stages of its development in the blood corpuscles is extremely active. Its unceasing restless changing of shape is fascinating to watch under the microscope and one feels that it was very appropriately named " vivax." Unlike the malignant parasites of æstivo-autumnal malaria, the tertian parasites do not tend to clump together, and so do not become plugged in the capillaries but remain constantly in the circulation. To this fact, as will be shown later, is due the " benign " nature of this and also of the quartan parasite. The tertian parasites have the peculiarity of growing very large and of causing the corpuscles which they parasitize to enlarge and become unhealthy in appearance. The number of spores which result from the sporulation every 48 hours ranges from 10 to 25. According to Ross the normal number of splits of the nucleus is four, which would result in 16 spores. One of the most striking points of difference from the " malignant " parasites is the fact that the gametocytes are not in the form of crescents, but are rounded.

The quartan parasite, *P. malariæ*, resembles the tertian parasite in flexibility of body and form of gametocytes, but it differs in that it does not cause the corpuscle to enlarge and is never active in movements. It produces only from five to ten spores, the nucleus normally undergoing three splits. The spores tend to form a regular rosette or " daisy-head," arranging themselves petal-like around the dark mass of pigment in the center. Unlike either of the other parasites this one causes ague by its sporulation once in 72 hours instead of in 48 hours.

Identification of Stages and Species. — The correct identification of the stages and species of malaria parasites as seen in smears of human blood is difficult at first, but becomes easier with experience; the differentiation between *vivax* and *malariæ* is more difficult than between either of these and *falciparum*. The forms that are likely to be found in the peripheral blood are the " ring " forms, representing very young individuals; growing schizonts; full-grown and dividing schizonts; and male and female gametocytes. In the case of *P. falciparum* only the rings and the gametocytes are likely to be met with in the peripheral blood.

The ring stages (Fig. 55, *1*) of *vivax* and *malariæ* are indistinguishable, but those of *falciparum* can usually be differentiated. The rings of the former species are relatively coarse and have a diameter about $\frac{1}{4}$ to $\frac{1}{2}$ that of the red cell; there is rarely more than one ring in a cell, and the rings are not frequently found perched on the edges of the cells, or with double nuclei. *P. falciparum* rings are smaller, only about $\frac{1}{6}$ the diameter of the cell, and finer, the cytoplasm being almost a hair line; they are very often perched on the edges of the cells, multiple infections of one cell are common in heavy infections, and rings with two nuclei are often met with.

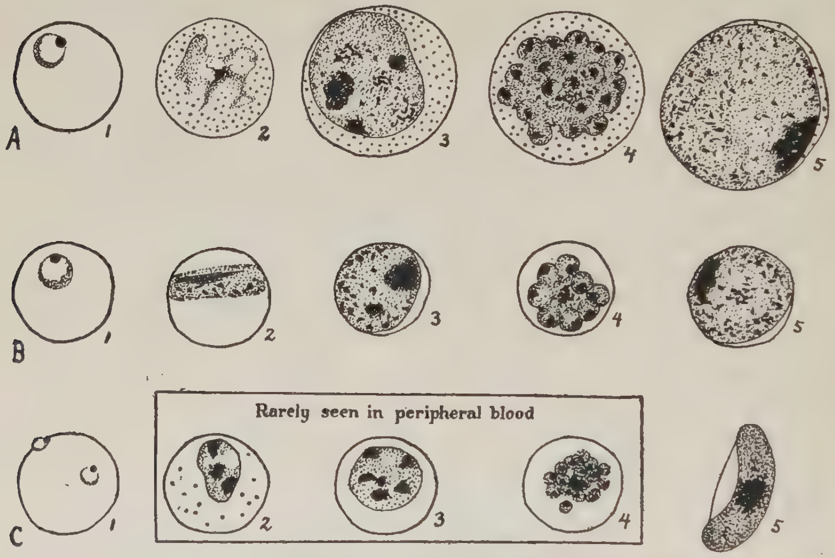

FIG. 55. Comparison of the three species of malaria parasites, illustrating diagnostic characteristics in each stage. A, *Plasmodium vivax;* B, *P. malariæ;* C, *P. falciparum;* *1*, "Ring" stages; *2*, growing schizonts; *3*, grown schizonts with dividing nucleus; *4*, segmenting parasites nearly ready to leave corpuscle; *5*, female gametocytes.

All later stages of the schizonts of *vivax* are recognizable by changes in the red cell which are not produced by the other parasites. The cells enlarge to about $1\frac{1}{2}$ times their normal size; they become pale; and, if properly stained with a Romanowsky stain, they are stippled with red dots called "Schuffner's dots." The growing schizonts (Fig. 55, *2A*) are characterized by their extreme irregularity of form, being "sprawled" all over the cell as a result of their active ameboid movement. The grown and dividing schizonts have a light brown pigment in rather fine granules. In *P. malariæ* the cells do not enlarge, do not turn pale, and do not show Schuffner's dots; the parasites are smaller (occupying about $\frac{2}{3}$ of a normal cell) and less irregular in shape, showing a tendency to the formation of bands extending across the cells (Fig. 55, *2B*), and the pigment granules as coarser and very much darker. These stages of *P. falciparum* (Fig. 55*C*, *2*, *3* and *4*) are only exceptionally found in the peripheral blood, but when found they resemble *P. malariæ* rather than *vivax*. In deeply stained films, corpuscles infected with *falciparum* show " Maurer's dots," which are coarser and fewer in number than " Schuffner's dots."

The gametocytes (Fig. 55, *5*) are the most useful stages for identification of the species of *Plasmodium*. Those of *vivax* and *malariæ* are more or less rounded, like the grown schizonts, but while the latter have the melanin granules collected into one or two clumps, and the nucleus usually is already divided, the gametocytes have the melanin granules scattered all through the body, as if peppered, and the nucleus shows no evidence of division. Female gametocytes stain a deeper blue than the males, and have a small deep-staining red nucleus which usually lies towards, or at, one side of the body; male gametocytes are pale and have a large pinkish nucleus which is variable in position but often streams across the equator of the body. The gametocytes of *P. vivax* are 10 to 14 μ in diameter, lying in an enlarged, pale corpuscle with Schuffner's dots, while those of *malariæ* are only about 7 μ in diameter, almost filling a red corpuscle which is neither enlarged nor pale, and has no Schuffner's dots. The pigment is blacker and coarser and tends to be concentrated peripherally and in a dense mass near the center. The gametocytes of *P. falciparum* are at once identifiable by their crescent shape. They are about 10 to 12 μ long and 3 to 4 μ wide. The females are longer and more slender than the males, stain deep blue, and the small red nucleus lies in a cluster of pigment granules near the center. The males are more squatty, stain more faintly, and the pigment granules are more scattered, though the poles of the crescent remain clear.

Propagation. — As a result of the work of Ross and Grassi, which set such an important milestone in the progress of preventive medicine, malaria is now known to be transmitted only, except in rare prenatal infections, by the bites of certain species of mosquitoes, all belonging to the genus *Anopheles* (including its subgenera). While over a hundred species of *Anopheles* have been described, only comparatively few are of any real importance in the transmission of malaria. This matter is discussed in the Chapter on mosquitoes (p. 563). As shown there, some species are eliminated because they do not readily nurse the malaria parasites through their sporogonic cycle; some are eliminated because of their habits; and others are of no importance on account of their rarity. Local conditions may influence the importance of particular species of mosquitoes in transmitting malaria, and therefore local epidemiological surveys to determine the prevalent transmitters are important. Since the different species vary greatly in their breeding habits, control measures must depend on the habits of the particular species involved. Malaria does not become endemic wherever suitable *Anopheles* mosquitoes occur; it requires a certain " density " of mosquitoes in order to insure the successful propagation of the disease. Ross has calculated that a relatively high number of malarial mosquitoes per person, probably between 40 and 60 per month, is required, and that a small deviation above or below the critical number may mean the difference between an ultimate extermination of the disease and its permanent establishment. Ross also shows that the relation between the amount of malaria in a given region and the number of malarial mosquitoes relative to the population is so definite that it can be mathematically computed.

Many " latent " cases of malaria develop in people in endemic regions. In these cases the parasites are so scanty that they cannot be found in the blood, and no symptoms are present. Such individuals may subsequently have a recrudescence of the disease as the result of exposure to sudden changes in weather, to fatigue, to dissipation, or to other sickness; a mere change of climate and environment, producing a temporary physiological shock, may be enough to precipitate active malaria in a latent case. Since such cases may occur in the entire absence of *Anopheles* mosquitoes, it is little wonder that a popular opinion still exists that malaria may be caused directly by these conditions.

Instances have been recorded of people developing malaria after visiting mosquito-infested places which were believed to be uninhabited, and in consequence it was suspected that there might be some animal reservoir of human malaria parasites. Although species of *Plasmodium* live in a variety of animals, including monkeys, bats, rodents and birds, some of which closely resemble one or another of the human species, these parasites are not infective for man when directly inoculated, nor can these animals be infected by inoculation of human parasites. The only exception to this is the case of one chimpanzee successfully infected with *P. vivax*. The evidence favors the view that apes *are* subject to human malaria, and suffer as a result of living too near human habitations. The possibility of transmission of human malaria to other animals by sporozoites from infected mosquitoes seems not to have been investigated.

It is clear that there are two factors necessary for the propagation of malaria, — infected human beings, and a fairly large number of suitable *Anopheles* to spread the infection. The number of oöcysts which develop on a mosquito's stomach is proportional to the number of gametocytes in the blood sucked, but only a small percentage of the gametocytes actually develop; many of them pass right through the mosquito's digestive tract. Temperature, too, has an influence. According to Grassi, the minimum temperature at which the microgametes are formed is about 65° F. Conflicting results have been obtained from experiments on the effect of intermittent or continuous cold on the development of the oöcysts in hibernating mosquitoes, and on the possibility of such mosquitoes carrying the infection through a winter. King in America and Wenyon in Macedonia have succeeded in exposing infected mosquitoes to low temperatures without destroying the parasites, whereas Mayne (Mitzmain) found that, in *Anopheles* infected prior to hibernation, the partially formed oöcysts degenerated, and sporozoites were not formed. The evidence is against the sporozoites, even if already developed before hibernation, surviving the winter, although this undoubtedly sometimes happens. Infective sporozoites survive in mosquitoes for at least several weeks after they have first become infective; James (1926) had one remarkable mosquito, which was caught on Aug. 5th and was finally dissected on Nov. 16th of the same year, with active sporozoites still in its salivary glands. In the meantime it had spent a hectic life in incubators, icebox, hospitals, railway trains, etc., and had successfully infected more than 40 general paralysis patients as a means of treatment! Humidity does not affect the development in the mosquito if the mosquito itself can survive, but Gill (1921) called attention to the influence of aridity on malaria by causing the death of mosquitoes before the sporozoites could develop.

According to Wenyon (1921, quinine taken by a patient affects the gametocytes of *P. vivax* so that they fail to develop in mosquitoes, but it does not affect those of *falciparum.*

The time required for mosquitoes to become infective is usually said to be 10 to 12 days, but it varies with the temperature. At 80° F. or higher the development takes 7 to 8 days, but there is a heavy mortality among the mosquitoes; as the temperature falls the time is increased; at 65° to 75° *P. vivax* requires 15 to 17 days, and *falciparum* about 19 days; below 65° *falciparum* gives up the struggle, but *vivax* still develops slowly down to about 60°, at which temperature it is estimated to require about 53 days

The Disease. — Malaria as a disease is extremely variable. A "typical" case of malaria, in the tropics at least, is a rather unusual thing. As we have seen, there are at least three different kinds of malarial parasites, each of which produces a somewhat different disease. While ordinarily all the parasites of a brood mature at regular intervals, a person in a malarial district may be infected with two or more broods maturing at different times, and the case may be further complicated by a " mixed " infection, that is, by more than one species of malaria at a time. Varying degrees of immunity, the effects of insufficient quinine or other drugs, the presence of complicating diseases and the virulence of the particular strain of parasites all have a hand in modeling the effects produced by malaria. It is little wonder that in some places practically every ailment or feeling of " malaise " is attributed to malaria. In the tropics such a diagnosis would be correct in a great many cases. However, the habit of attributing any indisposition which cannot be accounted for otherwise to malaria has been transplanted into non-malarial places, and it is not uncommon to hear of a person having a " touch of malaria " when in reality he has only indigestion, a cold or a light case of influenza. It is largely due to this fact that malaria is looked upon in non-malarial districts as of such small consequence.

The early stages of all types of malaria are similar except that the quartan type produces the intermittent fevers on every third, instead of every second, day. During the incubation period of the disease there is a feeling of ennui with headache and perhaps slight fever. After about a week, when the parasites have multiplied until there are about 200 per c.mm., which would total about one billion in the entire body, the regular intermittent fevers set in. Each attack begins with a shivering chill, sometimes accompanied by convulsions, so severe that the teeth chatter and goose-flesh stands out all over the body. Yet the temperature will be found to be several degrees above normal, and still going up. In the wake of the chill comes a burning and weakening fever, with violent headache and vomiting and a temperature from six to eight degrees above normal. The fever stage in turn is followed by a period of sweating, so profuse that the clothes or bedding may become wringing wet. The sweating gradually subsides, the temperature drops rapidly, often below normal, and the patient, after from six to ten hours in the case of benign infections and about 20 hours in malignant infections, rests fairly easily until the next attack. The fact that the attacks most commonly occur between midnight and noon, instead of in the evening, is often useful in distinguishing malaria from other intermittent fevers.

In the case of " benign " (tertian and quartan) infections after these agues have recurred for about ten days or two weeks, the symptoms gradually subside and the patient experiences a rally. From this point either he may recover completely (even if untreated) or he may suffer a relapse with all the old symptoms of regular agues. Then comes another rally and a second relapse, this continuing for months or years, aided, perhaps, by constant reinfections. During all this time general symptoms of emaciation, sallowness, anemia and enlarged spleen constantly increase at a diminishing rate with each relapse, and decrease at a similarly diminishing rate with each rally, so that eventually a fairly constant state of spleen enlargement, emaciation, anemia, sallowness and general run-down condition is arrived at — the well-known condition of chronic malaria, or malarial cachexia, common especially in children. The spleen enlargement is the most readily recognizable symptom of chronic malaria and therefore the "spleen rate," *i.e.*, the percentage of enlarged spleens in a community, gives a fairly accurate measure of the prevalence of malaria to which some degree of immunity has been developed. Usually, unless the weakened condition has given some other disease a chance to put an end to it all, a general improvement ultimately begins. This is especially true in children, so that by the time they reach adult life they are in fairly good health and immune to malaria.

In the case of æstivo-autumnal or malignant malaria the course of the disease is often not so light, and early death is not a rare occurrence. The fact that the bodies of the malignant parasites clump together and plug the capillaries, thus preventing the proper flow of blood in the vital organs, is probably the chief cause of their malignant nature. One of the most certain symptoms of a malignant attack of malaria is a total loss of consciousness, or coma, due to a plugging of the capillaries in the brain. Indeed, 50% of the deaths from malaria are said to be caused by a plugging of the brain capillaries. The type of brain disease which may be caused is very variable but some mental disturbance almost always occurs, and may take place at almost any time during the course of the disease, though it never occurs during the first fever fit, probably because the parasites are not yet numerous enough to do any great damage

The course of the disease is directly dependent on the behavior and fate of the parasites in the body. The recurring chills and fever coincide with the bursting of the infected corpuscles and release into the blood stream of the young living merozoites, of the residual protoplasm and waste products of the parent schizont, and of the remnants of the infected corpuscle. It was formerly thought that the melanin of the parasites acted as a specific poison, but the present view is that the poisonous effect is anaphylactic in nature, due to the liberation of foreign proteins, not necessarily poisonous in themselves, into the blood stream.

It is evident that a heavy destruction of malaria parasites takes place in the body even while the disease is developing. Knowles points out that a single parasite producing 20 merozoites at each successive multiplication, if unchecked, would have increased in 20 days to the point where there would be about four parasites to every blood corpuscle and the patient would certainly be dead. Obviously, therefore, the parasites do not have such a care-free time of it, and enormous numbers must be continuously destroyed. Eventually the rate of destruction exceeds the rate of reproduction, and the parasites get scantier until finally there is no reasonable chance of finding them by blood examinations. But as they get scantier the rate of destruction slows up, and there is therefore a revival in parasite numbers, followed by another set-back, etc., until an equilibrium is reached. Just how the destruction is accomplished is uncertain, but it is probably in part by antibodies in the blood, in part by phagocytosis, and in part by destruction in the spleen (which Knowles considers a grave rather than a birth-place of malaria parasites). In one way or another, however, the patient's powers of resistance reduce the infection. If, now, the powers of resistance are temporarily lowered by a cold, exhaustion, or some other devitalizing factor, the parasites at once take advantage of the breach, and a relapse follows. Back in 1902 Schaudinn explained the phenomenon of relapse by supposing that the gametocytes, which he thought were very long lived and were the only forms present in the interval between relapses, could, as it were, think better of their destiny and revert to schizogony, — in other words, undergo parthenogenesis, — and for years, in fact up to 1917, Schaudinn's explanation was accepted; apparently it did not occur to anyone that the offspring of a parthenogenetic gametocyte ought to be sporozoites and not merozoites.

Immunity and Epidemics. — Absolute immunity to malaria is rarely if ever acquired but, as already remarked, oft-repeated infections, especially in childhood, tend to build up a high degree of tolerance to the effects of the parasites and a diminution in the number of parasites in the body. The protection afforded by a single infection is very slight, and is retained for only a short time in the absence of reinfections. Even the cumulative effect of numerous infections disappears rapidly in the course of a few years. Some authors divide malaria into two types. There is a " tropical " form, occurring in places where reinfections can occur practically throughout the year on account of the continued warm temperature. The other, a " subtropical " form, is found in regions where cold weather causes an annual seasonal interruption of infection by a cessation of breeding on the part of *Anopheles*, and by a discontinuance of growth on the part of the parasites in the mosquitoes. In tropical malaria a fairly constant degree of immunity is maintained, and epidemics are rare if they occur at all. In Java and other tropical places, according to Robert Koch, nearly every native child, under four years of age, has his blood teeming with malaria parasites from which he suffers little inconvenience. These parasites gradually become scarcer in older children and are often practically absent in adults who, however, have been shown to be passive " carriers " of small numbers of the parasites and therefore a source of danger to the community. A similar condition has been described by Christophers (1925) in a highly malarial locality in India. He found that children in the first two years of life suffer from continuous malarial fever, and have an average of more than 10,000 parasites per c.mm. of blood; between the ages 2 and 5 the infection is still 100%, but there are only 1200 parasites per c.mm., and fever attacks about once in 25 days; between the ages 6 and 10 there is still 100% infection, but less than 1000 parasites per c.mm., and no fever; in adults there is 50% infection, but few parasites and full tolerance to the infection. The " carriers," though relatively immune to the more acute symptoms of the disease, are often left in the run-down condition of malarial cachexia. As pointed out by Gill, there is a striking analogy between the confirmed opium-eater and the malarial cachectic. Both have purchased their immunity at a heavy price. In the former the emaciated frame, sallow complexion and other signs of debility proclaim the victim of a drug habit; in the latter the enlarged spleen, the lack of physical and mental energy, and the shrunken body bear witness to the havoc wrought by long-standing malaria. In the case of neither does death often take place as the direct effect of their respective poisons, but both readily fall victims to intercurrent affections. In subtropical malaria, on the other hand, the average tolerance of the community to the disease suffers an annual relapse, and may constantly decrease for a number of years. When the immunity as a whole becomes quite low, and there is a sudden increase in the probability of infection by a great increase in number of mosquitoes, accompanied possibly by an influx of infected people, an epidemic of the disease may occur of such extraordinary severity as to involve almost the entire population, and to cause a mortality of several hundreds per thousand. Such devastating epidemics, nearly always of the subtertian type of malaria, have been termed " fulminant malaria " and occur in malarial countries lying just outside the region of " tropical " malaria. Fulminant malaria in especially severe form occurs periodically in parts of India and in Italy.

It was formerly thought that considerable racial immunity protected the negro races, but it has been shown that in many cases, at least, the immunity has been acquired by constant exposure to the disease, and that it disappears upon removal from infected regions. The whites in southern United States are said to suffer markedly more from malaria than do the negroes though the latter are more frequently parasitized, but this may be due, in part at least, to the more permanent residence of the latter in the malarial districts.

Treatment. — Nearly three centuries ago, in 1640, a countess returning to Europe from Peru brought with her some bark from a cinchona tree, an infusion of which had been used by the native Indians to cure an attack of malaria from which she suffered. The value of the drug was established at once, and for nearly three hundred years the essential principles of cinchona bark, — quinine and allied alkaloids, — were practically without competition as remedies for malaria. It is doubtful if there is any other remedy known to man which has saved as many lives or relieved as much suffering. In 1926, however, German chemists produced a synthetic drug, plasmochin, which is basically similar to the cinchona alkaloids, and which is coming into great prominence as an alternative anti-malarial drug. It is quite likely that, as happened with synthetic arsenic and antimony drugs, other modifications of the drug will be produced which may be even better; plasmochin is probably the beginning, not the end, of synthetic anti-malarial drugs.

Cinchona bark contains a number of alkaloids, all of which have a more or less specific effect on malaria parasites, some more than others. Quinine has been singled out for the treatment of malaria, although others of the alkaloids, especially quinidine, are apparently even more effective, though slightly more toxic. In recent years "cinchona febrifuge," which contains a mixture of the cinchona alkaloids, has been largely substituted, in India, for the more expensive, and if anything less effective, quinine.

The effect of quinine and the related alkaloids on malaria is remarkable, — the organisms disappear from the blood and symptoms are alleviated almost at once, but, as in the case of other chemical substances used for protozoan diseases, the magical improvement is misleading; relapses occur unless the treatment is persisted in. Bass recommends a standard treatment of 10 gr. of quinine sulphate by mouth three times a day for three or four days, followed by 10 gr. every night before retiring for eight weeks. There are a number of factors which influence the effectiveness of quinine, such as the alkalinity of the blood and of the intestine, which can be turned to advantage by the administration of alkalis or citric acid with the drug, selection of the proper interval after meals, etc. The importance of these considerations seem not to be appreciated by many practitioners. Sometimes very speedy action is needed, and it is not safe to wait for quinine to be slowly absorbed from the stomach. Many a patient has died from malaria with enough quinine in his stomach to have saved his life had it been properly given. In such cases injections into the muscles, or still better, directly into the veins, is necessary. In malignant malaria quinine does not reach the parasites plugged in the capillaries and therefore can destroy them only as they sporulate and get back into the circulation. Since the parasites of this type often sporulate at irregular intervals a constant supply of quinine at a killing concentration must be kept in the blood. However, overdosing with quinine is not an uncommon fault with physicians. Quinine poisoning in some respects resembles malarial symptoms and the physician, thinking the latter are not abating, gives still more quinine until the patient succumbs to it. Not a few malarial deaths are really due to excessive quinine. Quinine must be avoided during or immediately following an attack of blackwater fever, since the symptoms of this malady are intensified by its use.

In case of severe malarial cachexia, the only safe course is for the patient to leave the malaria-infected country in which he has been living, and stay away for an extended period of time. He should take regularly small doses of quinine to kill any lurking parasites which may remain in his body, and do everything possible to build up his general health and to regain his lost vitality.

Quinine has very little effect on the gametocytes of the malaria parasites. Plasmochin, on the other hand, has a marked effect on them, even on the crescents of *P. falciparum*, which are especially resistant to quinine, and therefore this drug is very valuable as a means of sterilizing the blood to prevent infection of mosquitoes. Plasmochin, in tolerated doses, appears to be more effective against *P. vivax* and *malariæ* in all their stages of development than is quinine, whereas, although it is usually destructive to the crescents of *P. falciparum*, it has a weak action against the schizonts of this species, and so is not as valuable for cure as is quinine. A compound of plasmochin and quinine is recommended for malignant tertian malaria, on the theory that the quinine will kill the schizonts and the plasmochin the gametocytes.

Prevention. — The prevention of malaria is a problem that should be solved not by individuals but by civic effort. Ross says: " It (malaria) is essentially a political disease — one which affects the welfare of whole countries; and the prevention of it should therefore be an important branch of public administration. For the state as for the individual health is the first postulate of prosperity. And prosperity should be the first object of scientific government.'' But governments are notoriously slow in making large investments in public health, even if assured of ultimate large returns. Many of the most brilliant examples of malaria control have been executed by private industrial organizations and business concerns, which have been quick to see the importance of protecting the health of their employees as a business proposition solely.

Since malaria parasites have two hosts, man and mosquito, the possibility of exterminating them in either host presents itself. Some workers have advocated wholesale " quininization " to eliminate the parasites in the human host. As an adjunct to mosquito control this method is often valuable, but the large number of partially or entirely immune carriers makes the complete eradication of the disease by this means very difficult if not impossible, and every newcomer is a source of danger. Plasmochin is a better blood sterilizer than quinine, on account of its immediate action on the gametocytes.

As a personal preventive measure, prophylactic daily doses of quinine are often taken, 5 to 10 gr. per day. As long as kept up this prevents an attack of malaria, but it does not prevent infection, and often, soon after a person has left a malarial district and stopped the routine quinine, he comes down with fever. This can only be prevented by intensifying the prophylactic treatment for two weeks or so after leaving an endemic locality. Much personal protection can also be obtained from adequate screening and favorable location of residences.

Malaria can seldom if ever be permanently controlled except by fighting malarial mosquitoes. Although malaria affects large areas of a country, the problem of control is essentially local; the methods which are effective in one locality may be worthless in another. A malarial survey is *always* required before intelligent control measures can be instituted in any locality. This consists in mapping the locality to show distribution of population, malaria cases, Anopheles breeding places, etc.; collection and breeding out of Anopheles larvæ, and collection and dissection of adults; determination of the spleen rate; and determination of both incidence of parasite carriers and average numbers of parasites per c.mm. of blood. The results of the survey will not only indicate the local facts with respect to epidemiology, but will furnish a standard of measurement of improvements brought about by the control measures used. Excellent books on the control of malaria have been published by Watson (1915) (1921), Le Prince and Orienstein (1916), Hardenburg (mosquito control) (1922), and Christophers, Sinton and Covell (1928). Some of the outstanding examples of accomplishments in malaria control are the work of Grassi and others in Italy, of Ross at Ismailia, of Gorgas in Panama and Havana, and of Watson in Malaya. Almost magical results have been obtained in the way of reduced death rates, decreased sickness, and increased efficiency and health. Watson was so impressed by the decrease in deaths due to other conditions than malaria, following malaria control in Malaya, that he wondered what unrecognized malign influence had been eliminated along with the malaria, until he realized that it was chronic unrecognized malaria itself which had been the underlying cause of the "other deaths."

The problem of control resolves itself very largely into mosquito control, the main features of which — such as drainage, diking, oiling, fish-stocking, and Paris green dusting — have been briefly discussed in Chapter XXVII. Some workers have found evidence that malaria tends to disappear automatically in communities that reach a fairly high economic, social and cultural level. The Anti-malarial League of Greece has vouchsafed the opinion that widespread malaria was not the cause of the downfall of Greece, but was the result of it. Others believe that most of the malaria is due to a relatively small number of house-loving, well-protected, lazy female *Anopheles*, and that the thing to do is to catch and kill these. These factors very likely come into play in some localities and under some circumstances, but the great demonstrations in the possibilities of malaria control have accomplished their results by careful surveys of local conditions, followed by intelligently applied anti-mosquito measures.

Blackwater Fever

In many parts of the world where severe malignant tertian malaria is present, but not in all, there occurs a disease which is known as blackwater fever, about the real nature of which there has been more argument, and less definite knowledge, than almost any other human infection. It is a veritable scourge in many parts of Africa and in some parts of India, Malaya and the East Indies, and occurs in parts of southeastern Europe and in the southeastern United States. In many of these places it appears to be a rather recent development. The disease is characterized by a fever accompanied by an intense jaundice and a tremendous destruction of red blood corpuscles and excretion of hemoglobin in the urine. The number of blood corpuscles may be reduced by as much as 2,000,000 per c.mm. in two days.

There are several views with respect to the nature of blackwater fever, with good arguments both for and against all of them. These are very well reviewed by Yorke (1922). One view is that the disease is caused by a specific parasite, perhaps related to the Piroplasmata, which cause blackwater fever in cattle, but nobody has ever found such a parasite, whereas there is little evidence that blackwater fever ever occurs in the absence of an infection with malignant tertian malaria. Another view is that it is nothing but malignant tertian malaria endowed with exalted virulence. Thomson (1924) adduces excellent evidence in favor of this theory, but fails to make it clear why in some malarial countries blackwater fever is common and in others is unknown. No one can doubt but that *Plasmodium falciparum* has a hand in the proceedings somehow, — but perhaps it is only as a predisposing cause. A third view is that the disease is a manifestation of quinine poisoning or of this in combination with a prolonged malaria infection, but there seems to be well-authenticated records of blackwater fever in people who had not taken quinine. Whatever causes the sudden and devastating destruction of the corpuscles affects the malaria parasites almost as rapidly. In spite of the most persistent investigation by innumerable workers, blackwater fever is still a mystery.

CHAPTER X

OTHER SPOROZOA, AND OBSCURE OR INVISIBLE PARASITES

Coccidia

The Coccidia belong to the same order of Sporozoa as do the malaria parasites, but are placed in a separate suborder. Although in a general way their life cycles are similar they differ in that (1) there is usually no alternation of hosts for the sexual and asexual cycles, and (2) the zygote is a motionless body which forms a cyst and does not grow in size. The Coccidia with which we are concerned belong to the family Eimeriidæ. These parasites undergo schizogony and gametocyte formation in the tissue cells of their hosts; fertilization of the macrogametes by the sperm-like microgametes occurs in the same host, usually outside of the cells; the zygote then develops into a resistant oöcyst which leaves the body of the host; and the oöcyst develops within it, by a process which varies in different genera, the sporozoites which cause infection when the oöcyst gains access to a new host. In most genera sporocysts, which are "cysts within cysts," are formed inside of the oöcysts, and each sporocyst contains a definite number of sporozoites. The life cycle of a typical coccidian is shown in Fig. 56. Most of the coccidians inhabit the epithelial cells of the intestine, and only the oöcysts, which leave the body with feces, are usually seen. These are thick-shelled and might easily be mistaken for small worm eggs, since the characteristic sporocysts and sporozoites usually do not develop until some days after leaving the body. It sometimes happens that oöcysts of coccidians are eaten with the infected organs of animals in which they are parasitic, and species which are parasitic in the liver of herrings and in the testes of sardines have been mistakenly described as human parasites.

The true human coccidia belong to the genera *Isospora* and *Eimeria*. *Isospora* is characterized by the development, in the oöcyst, of two sporocysts each with four sporozoites, while *Eimeria* has four sporocysts each with two sporozoites.

Several species of *Isospora* occur in cats and dogs, others in birds, and others in reptiles and amphibians. The only species of which oöcysts are found in human feces is *I. belli*, which came to light during the Great War; nearly all the cases occurred in individuals who had been in contact with Turks in the Near East, and Wenyon thinks that Turkey may be the endemic home of the parasite, whence it has spread since the war to other parts of the world. The oöcysts are 25 to 33 μ long and about half as wide, with a slight neck-like constriction near one end (Fig. 57).

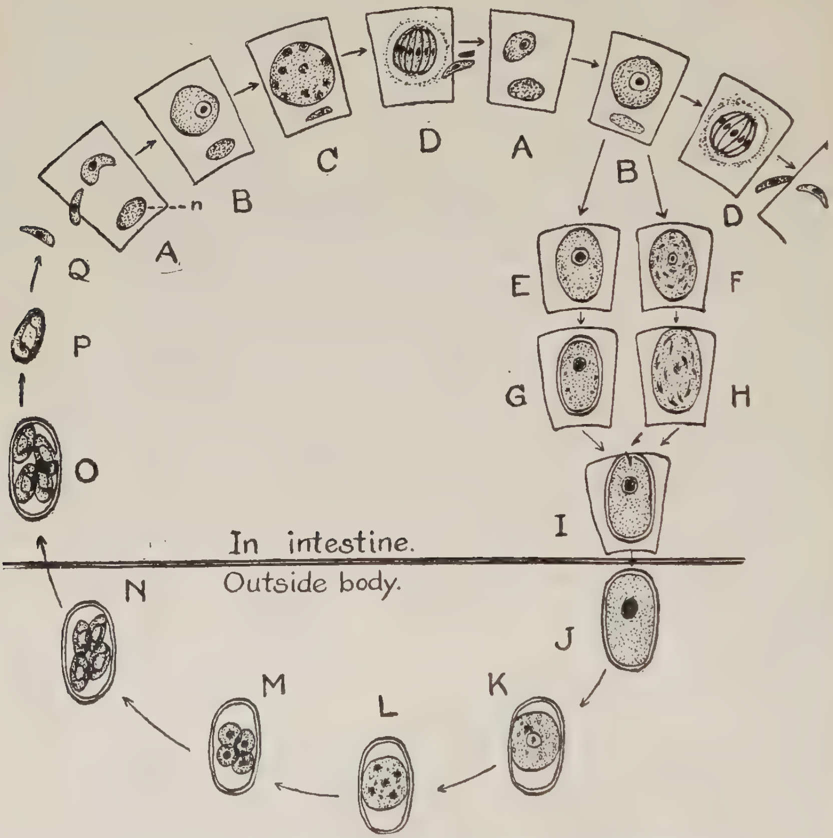

Fig. 56. Life history of *Eimeria* of bird. *A*, infection of epithelial cells of intestine by sporozoites ingested with food or water; *B*, growth inside cell; *C* and *D*, sporulation and formation of young spores; *E* and *G*, formation of female gamete; *F* and *H*, formation of male gametes; *I*, fertilization; *J*, fully developed oöcyst as passed out with feces; *K*, *L* and *M*, formation of four sporocysts; *N*, complete development of sporocysts, each containing two sporozoites; *O*, same, ingested by susceptible animal; *P*, sporocyst liberated from oöcyst in alimentary canal; *Q*, liberated sporozoite ready to infect epithelial cell, as shown in *A*.

They are transparent and colorless in fresh feces, with a spherical body inside. Subsequently this divides into two spherical bodies, the sporoblasts, which develop cyst walls, thus becoming sporocysts, measuring 12 to 14 μ by 7 to 9 μ. The sporoblast within each sporocyst now divides into four sporozoites and a large residual food body. The sporozoites are elongated, rounded at one end and tapering at the other. The entire development is completed in from one to several days, according to temperature.

Nothing is known of the asexual cycle of development of this species in the human intestine but it is probably like that of *I. felis* of cats. In this the merozoites enter epithelial cells of the villi, where they grow to about 12 μ in length and produce usually eight nuclei; division into eight or rarely sixteen merozoites now occurs, and these infect other cells. The macrogametocytes, formed from some of the merozoites, grow to large ovoid cells 25 to 35 μ long, around which a thin cyst wall forms while it is still in the tissues, but the thick resistant wall forms after it has fallen into the lumen of the intestine. The microgametocytes grow to 20 to 30 μ in length, and their nuclei divide into an enormous number of parts. Eventually an equivalent number of minute sickle-shaped microgametes, each provided with a pair of flagella, are formed in the mother cell. Fertilization probably occurs in the lumen of the intestine, the sperm-like microgamete entering an oöcyst through a little pore, the micropyle, at one end.

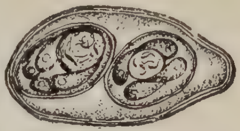

FIG. 57. Oöcyst of *Isospora* from British soldier returned from Gallipoli. Note presence of only two sporocysts, each with four sporozoites. ×1000. (After Wenyon.)

Another species of *Isospora*, *I. hominis*, which corresponds to *I. bigemina* of cats, probably occurs in man but has only rarely been observed, since the oöcysts are presumably formed in the deeper tissues of the villi and are not commonly found in the feces. The oöcysts of *I. bigemina* are about half the size of those of *I. felis*.

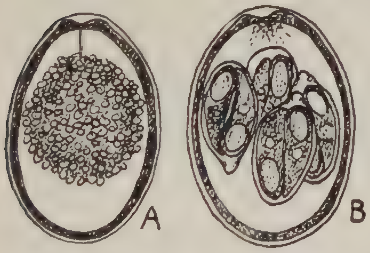

FIG. 58. Oöcysts of *Eimeria stiedæ*; *A*, undeveloped cyst as passed in feces; *B*, matured cyst with four sporocysts, each with two sporozoites. Note thick shells, with "micropyle" at one end. × 1000. (After Reichenow, from Wenyon's "Protozoölogy.")

Members of the genus *Eimeria* have made themselves at home in almost every kind of vertebrate, especially herbivorous ones, and in many invertebrates. In cold-blooded animals the oöcysts mature before leaving the host, while in warm-blooded ones they mature afterwards. *Eimeria* infections are extremely common in rabbits, and very often in mice also. Rabbits harbor one species in the liver and four, according to Kessel, in the intestine.

There are five cases on record of infection of the human liver with *Eimeria*, and it is generally believed that these were accidental infections with the liver parasite of rabbits, *E. stiedæ.* The oöcysts of *E. stiedæ* (Fig. 58), undeveloped in fresh feces, measure from 20 to 40 μ in length. The life cycle is essentially the same as in *Isospora.*

Little is known about the effects of coccidian infections in man. In an accidental laboratory infection described by Connal (1922), diarrhea and abdominal discomfort developed six days after infection, which lasted for four weeks and then disappeared along with the infection. In animals coccidians often produce extensive destruction of the epithelium of intestine or liver ducts, with diarrhea or dysentery which may be fatal. If the animal survives the acute attack the infection usually becomes chronic and mild, often with no evident symptoms at all.

Other Sporozoa

Although there are no other Sporozoa which are normally parasitic in the human body, it is appropriate here to mention briefly the third suborder of the Coccidia-like Sporozoa, the Piroplasmidea, because they are found in almost all kinds of mammals *except* man, and because from time to time structures are described from human blood smears which are interpreted as Piroplasmids or at least as related to them.

There are two types of Piroplasmids, (1) *Babesia* (Fig. 59*A*), which multiply in the red blood corpuscles by division into two or four, and tend to arrange themselves in couples; and (2) *Theileria* (Fig. 59*B*), which multiply by schizogony in endothelial cells of blood-vessels and finally invade red cells, where they occur as single minute bodies of various form; these are possibly gametocytes. Both are transmitted by ticks. *Babesiæ* cause many important diseases of domestic animals which are characterized by fever, rapid destruction of blood corpuscles, jaundice, and hemoglobin in the urine, whence the name red-water fever. It is interesting to note that the first instance of the transmission of a protozoan disease by insects was a demonstration by Smith and Kilbourne of the transmission of *B. bigemina* of Texas fever by ticks. *Babesia* diseases of great economic importance occur particularly in cattle, horses, and dogs, but infections also occur in sheep, goats and pigs, and in monkeys and many small mammals. *Theileriæ,* on the other hand, cause fever which is often fatal, without the accompanying jaun-

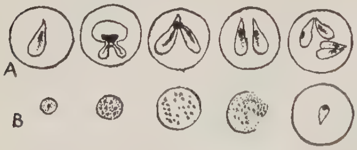

FIG. 59. *A, Babesia bigemina* (cause of Texas fever of cattle) showing multiplication in blood corpuscles. (After Nattall and Graham-Smith.) *B, Theileria parva* (cause of African East Coast fever of cattle) showing schizonts from the spleen, and an infected corpuscle. (After Nuttall.) Both × 1500.

dice and hemoglobinuria. They cause the deadly East Coast Fever of cattle in Africa. A similar disease occurs among sheep and goats.

A supposed parasite of the Japanese disease tsutsugamushi has been described by Hayashi (1920), together with a complicated life cycle, and referred to the genus *Theileria*. It is by no means certain that the structures described are organisms at all, much less *Theileria*, but it is possible, as Wenyon suggests, that they represent structures similar to *Rickettsia* or *Grahamella* (see pp. 186 and 191).

Sarcosporidia

This is a group of muscle-inhabiting, spore-forming protozoa the affinities of which are unknown; for a long time they were kept in company with the Cnidosporidia, largely for want of a better place. All the species are placed in a single genus *Sarcocystis*. The majority of them live in the striped muscle fibers of mammals and are especially common in sheep, cattle and horses. They consist of elongate, chambered bodies filled with sickle-shaped spores, which vary in size from young microscopic forms up to white streaks 5 cm. long (Fig. 60). Microscopic examination shows that these bodies are divided into numerous little compartments, more of which keep forming on the outside, while the older ones in the center finally break down. The smallest peripheral compartments contain single round cells; these divide into groups of cells which ultimately transform into the sickle-shaped spores, 10 to 15 μ

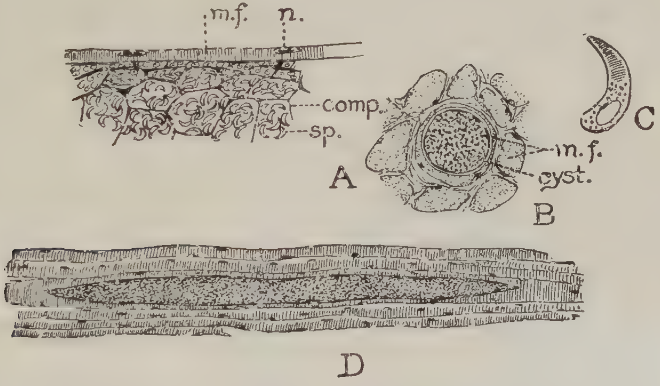

FIG. 60. Sarcosporidia. *A*, *Sarcocystis blanchardi* of ox, longitudinal section of infected muscle fiber (*m. f.*) showing spores (*sp.*) in chambers of compartments (*comp.*); *n.*, nucleus of muscle fiber; × 265. (After von Eecke from Wasielewsky.) *B*, cross section of sarcocyst from human larynx, probably *S. tenella*, × 200. *D*, same, longitudinal section. (After Baraban and St. Rémy.) *C*, spore of *S. tenella* of sheep. (After Laveran and Mesnil.)

in length (Fig. 60*C*). Infection can be produced by feeding spores to animals; this explains infection in flesh-eating animals but does not account for their prevalence in cattle and sheep. Spores are sometimes found in blood smears of infected animals, which suggests the possibility of transmission by blood-sucking flies.

Light infections seem to be borne without ill effects, but heavy infections may cause death. It has been shown that the parasites produce a very powerful toxin, called sarcocystin, which will kill rabbits in very minute doses. Erdmann suggests that the toxin, liberated in the intestine, may destroy epithelial cells and thus break a portal of entry for the young parasite. The cycle of development from time of infection up to the development of the cysts in the muscles is unknown; Crawley (1916) describes a sexual phase analogous to that of coccidians, but his interpretations have not been generally accepted.

Human infections are rare and only about a half-dozen authentic cases have been recorded. It is probable that the human cases are accidental infections with species belonging in other animals. Possibly they represent *S. muris* of mice, transmitted through food contaminated by the droppings. The use of infected meat seems to have no injurious effect.

Brief mention should be made of a parasite named *Rhinosporidium seeberi*, which was formerly regarded as an aberrant protozoan possibly related to the Sarcosporidia, and which causes polyp-like growths in the nose of man and horses. Ashworth (1923) showed definitely that this is really a fungus-like organism and not a protozoan at all.

Parasites of Obscure Nature

Rickettsia-like Organism

Organisms which have been called *Rickettsia* have been found in a great variety of arthropods, both blood-sucking and non-blood-sucking forms, and are found either on the surface of the gut epithelium, as in the case of *R. pediculi* of lice, or inside the cells of the gut epithelium or of other tissues. In either case they are transmitted hereditarily through the eggs to subsequent generations of insects, which shows that even the extracellular forms must have an intracellular phase of development. Sheep ticks or keds, *Melophagus ovinus*, are almost invariably hosts for an intestinal *Rickettsia* which is harmless to vertebrate animals. Some of the extracellular forms described in insects may be ordinary small bacteria adapted to life in insects. Among the described intracellular forms are some which appear to be necessary commensals without which the insects are unable to exist. *R. lectularia* of bedbugs, for instance, inhabits various organs, and in addition a special mass of tissue situated near the sex glands, apparently evolved especially for the purpose of harboring these symbiotic organisms. Many insects have such special "servant houses," called mycetomes, for the accommodation of symbiotic organisms which seem to be necessary to their lives, but most of these organisms are much larger than the *Rickettsiæ*.

There are three human diseases which are quite certainly caused by *Rickettsiæ,* and a fourth probable one. Two of them, typhus and spotted fever, are caused by intracellular forms in lice and ticks respectively, while one, trench fever, is caused by an extracellular intestinal form found in lice; the Japanese disease tsutsugamushi is probably also caused by a *Rickettsia.*

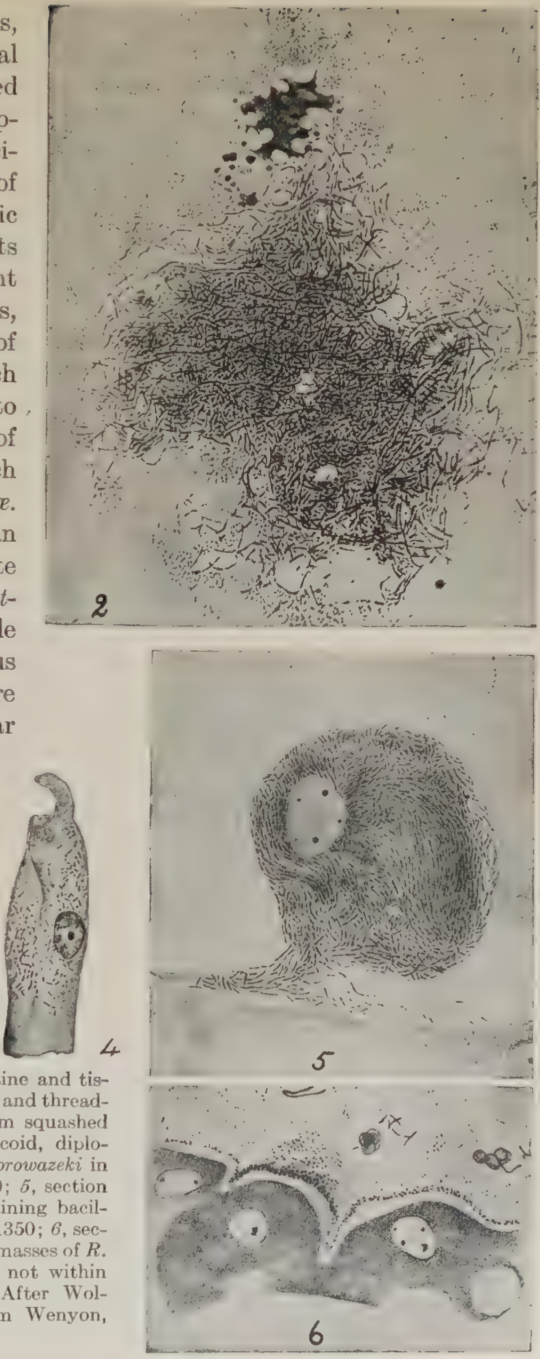

FIG. 61. *Rickettsia* in intestine and tissues of lice; *2,* granular, paired and threadlike forms of *R. prowazeki* from squashed intestinal cell, × 900; *4,* coccoid, diplococcoid and rod forms of *R. prowazeki* in section of intestinal cell, × 900; *5,* section of swollen intestinal cell containing bacillary forms of *R. prowazeki,* × 1350; *6,* section of intestinal wall showing masses of *R. pediculi* on the surface of but not within the intestinal cells, × 900. (After Wolbach, Todd and Palfrey, from Wenyon, "Protozoölogy.")

Typhus. — This disease, a guerilla of war, ordinarily slumbers in an endemic or latent state in those countries where the God of Cleanliness is not worshipped, and breaks forth into terrible epidemics when wars or other abnormal conditions afford opportunity for its rapid spread. In its endemic state the mortality is very low, *e.g.*, the so-called "tabardillo" of the Mexican plateau, but in epidemics it may kill 50% to 75% of its victims. The disease has a sudden onset, and is characterized by high fever, headache, rheumatic pains, bronchial troubles, congestion of peripheral blood-vessels, and a red rash later giving rise to dark blotches.

The exclusive transmission by lice was proved by Nicolle and his colleagues in 1909 (see p. 471). Ricketts first called attention to the minute granules in the intestinal cells of infected lice, and they were further studied by Prowazek and Rocha-Lima; the latter worker named them *Rickettsia prowazeki.* The organisms occur first as bacillary or filamentous structures in the cells of the gut, and subsequently produce minute granule-like bodies, and still later paired forms, like minute diplococci. Similar bodies are found in the endothelial cells of blood-vessels of infected animals, where the lesions are located. Lice which become infective invariably show typical *R. prowazeki*, whereas those lice which fail to become infective show no *Rickettsiæ.* There is, however, a strain of intracellular *Rickettsia* in lice which is not associated with typhus, and is called *R. rocha-limæ;* according to Weigl (1924) it can be differentiated from *R. prowazeki* in several ways. It spreads rapidly from louse to louse without apparently injuring them, while *R. prowazeki* infections are obtained only from typhus patients; the typhus *Rickettsia* is often fatal to lice, but it does not spread among them. Evidence of hereditary transmission is uncertain.

Trench Fever. — This disease, which was unknown before the Great War, but which was one of the most important diseases afflicting troops participating in it, was shown in 1918 by a commission of the Medical Research Committee of the American Red Cross, and also by a British committee, to be normally transmitted by body lice (see p. 473), although the possibility of transmission by body excretions also exists. A form of the disease occurring in Central Europe is known as Volhynian fever.

After an incubation period which is probably usually between 14 and 30 days, there is a sudden onset of fever accompanied by headache, dizziness, muscular pains, and other symptoms. The fever may last continuously for several weeks, or it may be more or less definitely relapsing. In most cases the spleen is enlarged, and there is a rash on the back, chest and abdomen. Usually the patient recovers after several weeks, but the illness may be greatly prolonged.

Toepfer, in 1916, discovered in lice taken from trench fever patients *Rickettsia*-like organisms which developed in the lumen of the gut, attached in masses to the epithelial cells; soon after, however, Munk and Rocha-Lima found similar organisms in presumably normal lice. They have not been found with certainty in the blood or tissues of patients. The best evidence for the relation of this extracellular *Rickettsia* to trench fever is an accident which happened to Bacot. These *Rickettsiæ* were found commonly in lice collected from a public bathhouse in Warsaw. Bacot acquired some of these lice accidentally and developed a typical case of trench fever. At this time he was feeding on his person a stock of lice brought from England, which were known to have been free from *Rickettsiæ* for over two years. Eight days after Bacot's attack of trench fever the lice he was nourishing began to pass *Rickettsiæ* in their feces. He continued to infect " clean " lice which fed on him for three months after the disappearance of all symptoms. This affords a possible explanation for the finding of *Rickettsiæ* like those of trench fever in supposedly uninfected lice, for, as Wolbach (1925) remarks, it is justifiable to assume that every lousy individual in the countries where trench fever was prevalent during and after the war has been exposed to the disease, and probably has suffered from it. Therefore feeding experiments on persons who have lived in a trench fever region are not reliable. According to Wolbach's views *R. quintana*, the name given to the trench fever *Rickettsia*, is identical with *R. pediculi*, supposed to be a non-pathogenic form found in normal lice.

Another possible explanation was offered by the writer (1923). As already remarked, trench fever was unknown before the war, yet during the war it became so common as to have caused more sickness than any other disease except scabies. Where this new malady came from has caused many an epidemiologist to think furiously and speculate wildly. To the writer it seemed that the case was analogous in some ways with that of *Trypanosoma rhodesiense*. In peace times lice infected with *R. pediculi* were confined in their movements to families and schools, and were passed back and forth among people who harbored them from the earliest days of infancy. Such people would be more or less continuously infected with a strain of the organism which had no opportunity to enhance its virulence by passage through a series of susceptible non-immune people. As infants these people might have light un-recognized attacks and become immune, as happens with young calves infected with Texas fever, or they might even resist infection altogether. During the war hundreds of thousands of non-immunes who had never before been bitten by lice were exposed to their bites, and under these conditions one can easily understand how a virulent strain could be built up by a few passages through such people, just as happens in the case of pneumonia, typhus and probably most epidemic diseases, for it is probably in this way that epidemics usually get started. According to this reasoning *R. quintana* is a strain of *R. pediculi* with its virulence exalted. It seems to the writer significant that since the war little more has been heard of trench fever. Lice have again become restricted to perennially lousy communities, and non-immunes are no longer exposed, wholesale, to infection.

Rocky Mountain Spotted Fever. — For many years certain limited districts in the Rocky Mountain region of northwestern United States, particularly Idaho and Montana, have been known to be affected by this very serious disease. Its yearly occurrence in well-defined areas has given rise to panic and hysterical fear of entering the " haunted " places. Houses were deserted, land depreciated in value, and some of the richest valleys in the Northwest left unpopulated. In 1906 it was shown by Ricketts that the disease was invariably preceded by the bite of a common local wood-tick, *Dermacentor andersoni* (see p. 430, and Fig. 202), which was experimentally shown to be the intermediate host of the parasite. Wolbach in 1919 demonstrated the regular appearance of minute organisms, which he named *Dermacentroxenus rickettsi*, in the cells lining the blood-vessels of infected mammals, and also in nearly all the tissues of infected ticks. The organism shows several morphological types, but most frequently appears in infected animals as paired lanceolate bodies, the length of a pair being about 1 μ. In infected ticks the organisms undergo a definite sequence of changes as follows: (1) an intracellular bacillus-like form without chromatoid granules, in the cytoplasm of gut cells; (2) a small rod-shaped form with chromatoid granules, in both the cytoplasm and nucleus of practically all the tissues in the body; (3) a relatively large, lanceolate, paired form with chromatoid staining, similar to the organisms found in infected animals, which persists in the tissues, and notably in the salivary glands, long after the other forms are gone. The latter is found in the eggs of infected ticks, and gives rise to infection in the ensuing generation of ticks. Wolbach has no doubts of these structures being true organisms, and not by-products of infection, and he has succeeded in getting them to live and multiply in cultures made with plasma and living tissues.

It requires from two to ten hours' feeding for a tick to become infected, but after an incubation period of a few days it remains infective for indefinite periods. In man the incubation period is usually from four to seven days. The disease begins with a general feeling of illness followed by chills and aches. A constant fever gradually increases until the tenth or twelfth day, when death is likely to occur in severe cases.

In mild cases the fever gradually subsides during the five or six days following. Usually on the third day a rose-colored rash breaks out on the head and upper part of the body, followed a day or two later by a characteristic spotting of the arms and legs, and later much of the body, caused by the bursting of blood capillaries in the skin, from which the disease takes its name. The fatality is very high in some localities and very low in others. Possible reasons for this, together with a discussion of the relation of ticks to the transmission of the disease, and the features of its epidemiology, will be found on p. 431.

Other Possible *Rickettsia* Diseases. — The similar clinical nature of the Japanese disease tsutsugamushi, and the similar " pseudo-typhus " of Sumatra and related diseases in the Philippines and Queensland, (see p. 401), suggests that these diseases are also caused by *Rickettsiæ*. Megaw has evidence of the sporadic occurrence of a tick-borne, typhus-like disease in India, and similar sporadic cases occur in Africa, Malaya, and elsewhere. Megaw suggests that all of these diseases are related, and suggests the names louse typhus, tick typhus and mite typhus for the typhus-like diseases transmitted by these vectors.

Other Parasites of Obscure Nature

Mention should be made of certain other bodies which have been regarded as parasites. In moles and other small mammals there are often found dot-like or rod-like granules in the red blood corpuscles, to which the name *Grahamella* has been given. Some writers consider them merely granules formed by degeneration of hemoglobin. Even if they are organisms, there is no sound reason for considering them protozoa rather than bacteria. Of similarly problematic nature are the red-staining dots found in the blood corpuscles of cattle and other animals and named *Anaplasma*. Infections in which as many as 50% of the corpuscles show these bodies can be produced by inoculation, and immunity results, which argues in favor of their being real parasites, but their resemblance to the red granules called " Jolly bodies " in the red corpuscles of young and anemic animals, and believed to be remnants of nuclei, throws suspicion on them. Wenyon suggests that there is possibly an invisible virus producing anemia in cattle, one of the features of which is the production of numerous " Jolly bodies."

Bodies which somewhat resemble *Grahamella* occur in the red cells, and also in endothelial cells, of human beings infected with Oroya fever, of which verruga peruviana has been shown to be a clinical form. Oroya fever is characterized by an extreme and rapidly-developing anemia.

The organisms are minute round, or slender rod-shaped, motile bodies, which were named *Bartonella bacilliformis* by Strong *et al.*, (1915). Recently Noguchi (1926) has succeeded in cultivating them, and has done away with any doubt of their being living organisms, but there seems to be no good reason for considering them protozoa rather than bacteria. Although they can be transmitted by ticks, they are normally transmitted by certain species of *Phlebotomus* (see p. 514). Within the past few years much interest has been aroused by the discovery that rats and mice are almost always infected with an organism similar to *Bartonella*, named *B. murisratti*, but, except in rats under 4 weeks old, they are so scanty that they cannot be found. If, however, the rats are deprived of their spleens, the parasites are unleashed in full fury, and become abundant in 4 or 5 days. Their appearance is accompanied by a pernicious anemia in which the blood corpuscles fall to about one-third their normal number in 2 days, and the animals often die. The infection is transmissible by rat lice, *Hæmatopinus spinulosus*. These observations take on much interest in view of the fact that Schilling (1928) found similar bodies, which he called "erythrokonten" in 39 of 42 cases of human pernicious anemia. Kikuth (1928) found a similar rapidly-developing anemia

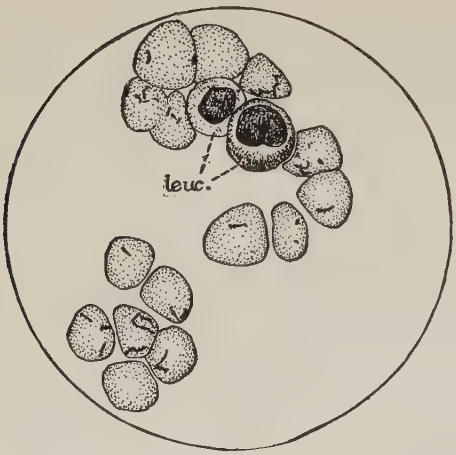

FIG. 62. *Bartonella bacilliformis* in stained blood from Oroya fever patient. Some cells show chains of parasites. Bodies with large dark nuclei are leucocytes (*leuc.*). × about 1000. (After Strong *et al.*)

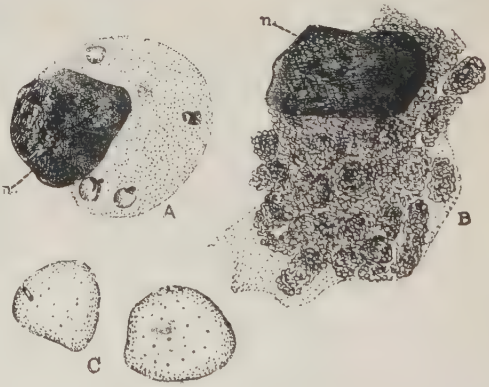

FIG. 63. Development of *Bartonella bacilliformis* in endothelial cells. *A*, endothelial cell, with large nucleus (*n.*) at left, containing five rounded bodies in early stage of development; *B*, endothelial cell showing rounded bodies developing large numbers of small rod-shaped parasites; *C*, red corpuscles lying near with parasites identical with those escaping from such a cell as shown in *B*. × 2000. (After Strong *et al.*)

with a *Bartonella* infection, which he named *B. canis*, in a dog following removal of the spleen. Occasionally these infections, ordinarily held at bay, get the upper hand under other conditions than removal of the spleen. Brumpt (1928) threatens to annihilate the name *Bartonella*, since he believes the organisms so named are nothing else than forms of *Grahamella.*

Another genus of organisms deserving brief mention is *Toxoplasma.* These are small elongate or crescent-shaped masses of cytoplasm with a central nucleus found in cells and body fluids, singly or in groups. They have been found in various mammals and birds, and can be inoculated from animal to animal, but nothing is known of their relationships. In 1914 Castellani described a *Toxoplasma pyogenes* from blood and spleen smears from a man who died in Ceylon, and two or three subsequent cases of what were supposed to be related organisms have been reported. Wenyon (1923) criticized these findings, believing, as do most others, that the objects found are yeasts or other vegetable cells which might have penetrated from the gut after death, or might have contaminated the smears by being present on the slides before the films were made, or in distilled water used in staining, or by falling on the smears from the air. Wenyon unreservedly says: " It is perfectly clear that no such parasite as *T. pyogenes* exists." Wenyon also believes that the " hæmogregarines " which have from time to time been described from man are of similar nature.

Filterable Viruses

There are a considerable number of very important human diseases which are caused by organisms so small that, at least in certain phases of their development, they are beyond the realm of visibility by any means now at our disposal. They are called filterable viruses because of their ability to pass through filters which ordinarily hold back visible bacteria. We must not, however, think of these filters as resembling miniature mosquito screens with meshes through which an organism absolutely can or cannot go. They should rather be thought of as sponge-like dams with pores of various size. Some of the so-called filterable viruses, and even visible bacteria, easily pass filters under certain conditions when they are held back under others. The temperature, pressure, duration of filtration, as well as the motility and slenderness of the organisms all have an influence. Another important factor is " adsorption," *i.e.*, a tendency, under certain conditions, for the protein molecules of the organisms, of enzymes, etc., to form loose chemical combinations with the filter so that they are held, more or less, as iron filings are held to a magnet. This happens especially when the medium is slightly acid. On the other hand, organisms can actually grow through a filter, or overcome the capillary attraction of the sides of the pores by their own motility.

There is no reason to suppose that all the " filterable viruses " form a natural group, or are in any way related to each other. Some of them show peculiar characters, such as resistance to certain physical and chemical agents, production of permanent immunity, stimulation of cell growth, failure to grow except in the presence of living cells, and production of " inclusion bodies " inside of affected cells (such as the Negri bodies of rabies, the Guarnieri bodies of smallpox and vaccinia, etc.) which afford some reason for considering them allied to each other, but whether related to protozoa, plants or bacteria no one can say, and some workers consider them self-perpetuating lifeless enzymes. Rivers (1928) and McKinley (1929) have given excellent accounts of the filterable viruses.

The " inclusion bodies," so-called because they are bodies which appear in the cytoplasm or nuclei of affected cells, are thought by some workers to be produced by the cell as a result of its attack by the virus, and by others to be phases in the development of the viruses themselves.

Some of the " inclusion bodies " have been regarded as protozoa, have been given specific names, and have been placed in a special group of protozoa, the Chlamydozoa. In the first edition of this book, in 1918, four diseases, — small-pox and vaccinia, scarlet fever, rabies and trachoma, — were considered under the heading Chlamydozoa in accordance with a very prevalent view of them by protozoölogists at that time. It is an interesting commentary on the march of progress to note that, of these four, there is strong evidence that two of them, scarlet fever and trachoma, are caused by bacteria of known types, and there is some similar evidence in the case of measles. The great difficulty comes in distinguishing between the true original cause and secondary invaders.

There is one group of the filterable viruses which needs special consideration, — a group transmitted by specific insects. The human diseases involved are yellow fever, dengue, and papatasi or three-days' fever. Their transmission by particular kinds of insects after an incubation period in the insects suggests that they may have a definite life cycle, and be related to the protozoa rather than the bacteria.

Yellow Fever. — Yellow fever was formerly the scourge of the Western Hemisphere, which many medical historians consider to be its original home; it occurs elsewhere only in West Africa. At one time there was no city on the whole Atlantic and Gulf coasts of the United States which was exempt from yellow fever epidemics. In New Orleans, for example, there have been epidemics which have cost thousands of lives and have terrorized the city; the last one occurred in 1905. During the French operations in Panama relay after relay of laborers were stricken with the yellow plague, and were turned loose to die without mercy or help, to be replaced by a new set. Engineers, nurses and doctors were likewise stricken. One vessel is reported to have brought over 18 young French engineers, all but one of whom died of yellow fever within a month after their arrival.

Hope dawned with the illustrious work of the American Yellow Fever Commission in Havana in 1900, consisting of Reed, Carroll, Lazear and Agramonte, the first three of whom lost their lives directly or indirectly as the result of their work. These men showed that yellow fever is not contagious but one which is transmitted only by the yellow fever mosquito, *Aëdes ægypti* (see p. 570). Although ordinarily transmitted by the bite, there is evidence that it can be transmitted by the feces also. Recent investigations in West Africa have shown that a number of related mosquitoes can also function as transmitters (see p. 570). As this book goes to press it is reported from South America that the bedbug has also been incriminated.

With this knowledge the disease has gradually been banished from its former strongholds, until today it exists in the Western Hemisphere only in limited parts of Brazil, though it still flourishes in West Africa. In 1918 Noguchi isolated a *Leptospira*, *L. icteroides*, from cases of supposed yellow fever in Peru, and it was thought that at last, after many false starts, the discovery of the organism of yellow fever had been achieved. Later work showed that Noguchi's spirochæte is probably none other than *L. icterohæmorrhagiæ* of infectious jaundice, and the true cause of yellow fever was demonstrated in West Africa to be an invisible filterable virus. The African work, like that in Havana, claimed three illustrious scientists as the price of the knowledge gained, and Noguchi, Young and Stokes were added to the list of yellow fever martyrs.

The disease is characterized by a short incubation period of three to six days, followed by severe headache and aches in the bones, and a sudden fever during which the face is flushed and swollen, and the skin dry. The fever slowly subsides, and after three or four days there is a period of calm, with the temperature near normal but the pulse very slow. By the third day the skin usually becomes a characteristic yellow color which deepens to a coffee brown. A striking but not invariable symptom, and one of ill omen, is the "black vomit," a gushing up through the esophagus of a coffee-colored or black fluid, consisting largely of fragments of red blood corpuscles and free hemoglobin, or sometimes pure blood. The period of calm may lead to recovery in a few days if death does not intervene, or there may be a second fever which lasts irregularly for a longer time than the first. One attack usually confers a life-long immunity.

The discovery that the Indian monkey, *Macacus rhesus,* is susceptible to experimental infection has already led to very valuable results, and will undoubtedly lead to more. A program of research is being steadily pushed forward by groups of well-trained, experienced, resourceful, and devoted men who do not hesitate to face isolation, hardships, and danger for the sake of human welfare.

Dengue. — Epidemics of dengue, seven-days' fever, or breakbone fever visit every part of the tropical and subtropical world. After an outbreak which often involves the majority of a local population it often dies out, to recur at irregular intervals, although in some countries it breaks out every year. The epidemics spread along the main trade routes, and spread inland from seaport towns. The epidemics usually spread with amazing rapidity, especially in localities which have been free for several years. Such an epidemic spread through Texas in 1922, accompanying an unprecedented outbreak of yellow fever mosquitoes, and it is estimated to have caused over half a million cases in about four months.

The disease has been shown to be transmitted exclusively by certain species of mosquitoes; a brief history of the development of this knowledge and an account of the mosquito primarily involved, *Aëdes ægypti,* will be found on pp. 570 and 575.

The disease begins with startling suddenness. Within a few hours a normal healthy individual acquires a prostrating fever, a severe headache, and terrible aches in the bones and joints which make it necessary to lie still. His face and sometimes his whole body becomes flushed and purple with congestion. In a day or two the fever moderates, and usually is terminated by a sudden crisis of nose-bleed and diarrhea, which relieves the congestion. A day or two of fairly good health intervenes, whereupon there is a return of fever and aches for a short period, accompanied by a measles-like rash, often of very short duration. Often there are lingering and recurring aches, especially in the knees and ankles, for several weeks before final recuperation, whence the name "breakbone fever." Uncomplicated cases are probably never fatal. Immunity is usually of very short duration, since more than one attack in a single epidemic have been known to occur.

Practically every fluid and organ in the body has been examined in an effort to find the organisms causing dengue. A number of supposed parasites have been discovered, but none have stood the test of later investigation. Couvy (1921) reported the finding of a spirochæte in the blood of some cases in Syria which he regarded as dengue, but which was transmitted by sandflies. De Faria observed similar organisms, and named them *Spirochæta couvyi*. Many extremely careful investigations by others, however, have failed to confirm these findings. Two possible explanations suggest themselves: the objects seen may have been artefacts resembling *Leptospira*, or actual spirochætes may have been found which were not, however, the cause of the disease. It is perhaps worth noting that both the writer and Knowles, in the same year, 1923, thought they had found a *Leptospira* causing dengue, but subsequently found that the supposed organisms, which had a remarkable resemblance to true *Leptospiræ* under dark field examination, were really only dancing filaments of fibrin.

On the other hand Ashburn and Craig (1907) showed that the virus was filterable, and this was fully confirmed by Siler, Hall and Hitchens (1926).

Chandler and Rice were able to transmit dengue experimentally by mosquitoes fed on patients from the first to fifth days of illness, and within 24 hours after feeding, but Siler *et al.* found an incubation period of eleven days necessary before transmission occurred, whereas Schule (1928) found eight days necessary (see p. 575). There seems to be no adequate explanation for these discrepant results, unless the infection can be hereditarily transmitted by mosquitoes to their offspring, and our mosquitoes were bred from stock already infected. Siler *et al.* got some evidence against hereditary transmission by mosquitoes, but the fact that papatasi fever is hereditarily transmitted makes the occurrence of such a phenomenon in dengue appear probable. The rapidity with which epidemics spread does not fit in well with an 8 to 11-day incubation period in the transmitting mosquitoes unless, as in sandfly fever, hereditary transmission occurs.

Papatasi or Three-Days' Fever. — Of the same general nature as dengue, but even milder, is papatasi, sandfly, or three-days' fever. Its geographic range is practically co-extensive with that of the sandfly which transmits it, *Phlebotomus papatasi*, — around the shores of the Mediterranean and through western Asia to central India. It occurs in annual epidemics which attack a high percentage of non-immune individuals.

The disease begins suddenly like dengue, with similar symptoms. The fever subsides, with relief of the congestion, about the end of the third day, but the patient remains mentally depressed and continues to have aches for a week or two longer.

There appears to be no certain way in which dengue and papatasi fever can be distinguished from each other except by the transmitting agent. Where both *Phlebotomus papatasi* and *Aëdes ægypti* occur together, the differentiation is practically impossible.

As with dengue, the germ is a filterable virus found in the blood of infected individuals. Many efforts have been made to find a spirochæte causing the disease, and some positive findings have been recorded. The patients in whom Couvy found a spirochæte were probably suffering from sandfly fever, and not dengue. Whittingham, in Malta in 1921–1922, cultured a spirochæte exactly resembling *Leptospira icterohæmorrhagiæ* from the blood of six patients, but the organism failed to cause disease in either non-immune human beings or in guinea pigs.

The blood of patients remains infective for only two or three days. There is an incubation period of about six days in the sandflies, and Whittingham has proved that the infection is hereditarily transmitted by the insects (see p. 510).

PART II — HELMINTHOLOGY

CHAPTER XI

INTRODUCTION TO THE "WORMS"

Classification. — The name "worm" is an indefinite though suggestive term which is popularly applied to any elongated creeping thing which is not obviously something else. There is hardly a branch or phylum of the Animal Kingdom which does not contain members to which the term "worm" has been applied, not excepting the great group Chordata, to which the backboned animals, including man himself, belong. In fact some animals, such as many insects, are "worms" during one phase of their life history, and something quite different during another.

In a more restricted sense the name "worm" is applied to three great groups of animals, with a few outlying forms, which superficially all resemble one another in being unquestionably "worm-like," though in life and structure they are widely different. To these animals, together with some other heterogeneous forms, the collective name "Vermes," meaning worms, was applied by the early workers on zoölogical classification. Upon more detailed study it became obvious that different types of the "Vermes" differed from one another very extensively. Some zoölogists split the "Vermes" into seven or eight distinct phyla or branches of the Animal Kingdom, but some still retain the majority of them in a single phylum Vermes, and consider the component groups as subphyla. The true segmented worms, which are more highly organized than any of the others, and are provided with a blood system and other specializations of structure, are universally recognized as worthy of separate rank, and are placed in a distinct phylum Annelida. One group of these, the leeches, are of interest as parasites. Of the remaining Vermes, two subphyla interest us as containing human parasites, namely the Platyhelminthes or flatworms, and the Nemathelminthes or roundworms. The former include the flukes and tapeworms, while the latter contain the nematodes and spiny-headed worms.

Flatworms. — The group of lowest organization is the Platyhelminthes. The worms included in this phylum are flattened from the dorsal to the ventral side, whence the common name "flatworms." Unlike nearly all other many-celled animals they have no body cavity, the organs being embedded in a sort of spongy "packing" tissue. The digestive tract in its simplest form, and as it occurs in the larval generation of flukes known as rediæ, consists of an elongated blind sac with only a single opening, serving primarily as a mouth and secondarily as a vent, but in most adult forms this sac is variously branched and in a few flukes even has an anus; on the other hand the tapeworms, constantly bathed in the semi-digested food of the host, have dispensed with the digestive tract entirely; the host does the digesting, and the surface of the body of the worm, functioning like the walls of the intestine of the host, does the absorbing. The nervous system is very simple, and the primitive ganglia which serve as a brain are located in the anterior portion of the worm. Performing the function of kidneys is a system of tubes, the terminal branches of which are closed by "flame cells," so called from the flamelike flickering of a brush of cilia which keeps up a flow of fluid toward the larger branches of the system and a posteriorly situated bladder, and ultimately to the excretory pore, thus conducting the waste products out of the body. The absence of any kind of blood system or other apparatus for transporting food or waste products in the body necessitates a branched condition of the digestive and excretory systems. The most highly developed system of organs and one which occupies a large portion of the body is that concerned with reproduction. Usually there is a complete male and female system in each worm and in some tapeworms there is a double system of each kind. In addition to the ordinary sexual reproduction of the adults, other additional methods of reproduction are resorted to by most flukes and by some tapeworms, in the form of parthenogenetic generations in the former and budding in the latter.

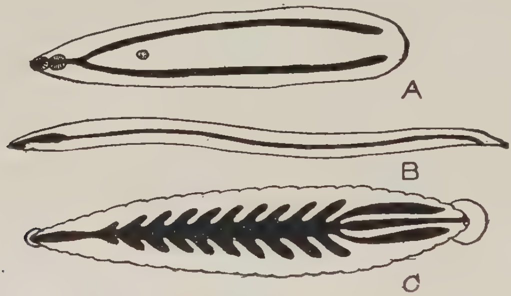

FIG. 64. Types of digestive tracts in worms; *A*, fluke, — note branching and absence of anus; *B*, roundworm, — note simple form, with only pharynx differentiated, and presence of anus; *C*, leech, — note extensive pouches or ceca which serve as reservoirs for surplus food.

The flatworms are usually divided into three classes, the Turbellaria, the Trematoda and the Cestoda, but modern zoölogists usually include also the Nemertea, a class of band-shaped marine worms of uncertain relationships, none of which are of interest in connection with human parasitology. The Turbellaria are for the most part free-living animals and include the "planarians" which can be found creeping on the under side of stones in ponds. The Trematoda include the flukes, all of which are parasitic, some externally on aquatic animals, others internally on aquatic or land animals. They are soft-bodied, flattened animals, usually oval or leaf-shaped, furnished with suckers for adhering to their hosts. The flukes which live as external parasites of aquatic animals have a comparatively simple life history, while those which are internal parasites have a complex life history, in the course of which they pass through two or three different hosts. The third class, Cestoda, is comprised by the tapeworms. As adults they are all parasites of the digestive tracts of various animals and are profoundly modified for this kind of an existence. Their peculiar method of multiplication by budding results in the formation of a chain of segments, sometimes of great length, which collectively constitute a tapeworm; each segment, however, is practically complete in itself and capable of separate existence if it had some method of retaining its position in the host's intestine. Some tapeworms have a life history comparable in its complexity with that of the flukes but as a rule it is much simpler.

Roundworms. — Of somewhat higher organization than the flatworms is the phylum Nemathelminthes, a term meaning "thread worms." These worms, with rare exceptions, are elongated and cylindrical instead of flattened, they possess a body cavity, and they lack flame cells. The majority of the included forms are true nematodes, belonging to the class Nematoda, but two other groups of worms, the Acanthocephala, or spiny-headed worms, and the Gordiacea, or horse-hair worms, are usually thrown in, largely for want of a better place to put them. Beyond a certain superficial resemblance in form, the Acanthocephala, at least, have little in common, either in structure or development, with the nematodes; they constitute a separate class. The "horse-hair snakes," which were for a long time popularly believed to develop out of horse hairs which fall into water, are exceedingly long and slender hairlike worms which live as parasites in insects until they become almost mature, when they emerge from the insects, usually after these are drowned, and reproduce in water. Occasionally they are accidently swallowed with drinking water and are usually promptly vomited, much to the surprise and horror of the temporarily infested person. These worms are grouped by some helminthologists as a separate class, Nematomorpha or Gordiacea, but others consider them a subclass of Nematoda, and give the name Eunematoda to the subclass which includes the true nematodes. The Acanthocephala are all parasites of the intestines of vertebrate animals and, like the tapeworms, are entirely devoid of a digestive tract, but are provided with a spiny proboscis which functions as a hold-fast organ, like the scolex of a tapeworm. The true nematodes have a very resistant chitinous cuticle, a simple digestive tract with mouth and anus, a fluid-filled body cavity which is not lined by epithelium as in other animals, and separate sexes, with the sex glands continuous with their ducts, in the form of slender tubules.

Annelids. — The most highly organized group of worms is the phylum Annelida, including the segmented worms or annelids. In three important respects these worms are the first animals in the scale of evolution to develop the type of structure characteristic of the vertebrate animals, consisting, namely, in a division of the body into segments, in the presence of a blood system, and in the presence of " nephridia " or primitive excretory organs of the same fundamental type as are the kidneys of higher animals. In addition the digestive system is highly developed and there is a well-developed nervous system distinctly concentrated in the head. In some annelids the sexes are separate, while in others both reproductive systems occur in the same individual.

At least three classes of Annelida are usually recognized, namely the Archi-annelida, including a few primitive marine forms; the Chætopoda, including the worms which are furnished with bristles or setæ, such as the earthworms and marine sandworms; and the Hirudinea or leeches, in which there are two suckers but no setæ. There are a number of other groups of worms which many zoölogists include with the annelids, but as their systematic position is doubtful and as they include no parasitic forms they need not be mentioned here. The only class of annelids which includes parasites of man is the Hirudinea or leeches. These animals superficially resemble flatworms but they can readily be recognized externally by the segmentation of the body; the internal anatomy is totally different. Both sexes are represented in each individual.

Parasitic Habitats. — As to the parts of the body which may be attacked by worms of one kind or another, there is hardly any organ or tissue which is exempt. There are flukes parasitic in man which habitually infest the intestine, liver, lungs and blood-vessels, and one species occasionally wanders to the muscles, spleen, brain and many other organs. Species occur in other animals with even more specialized habitats; there are some which inhabit the Eustachian tubes of sea cows, the frontal sinuses of polecats, the eye socket of birds, cysts in the skin of birds, etc. The adult tapeworms of man are all resident in the small intestine, but there are species in sheep and goats, and one in rats, which habitually live in the bile duct; larval tapeworms are found in a great variety of locations, — in the liver, spleen, muscles, subcutaneous tissues, eye, brain, etc. The majority of the parasitic nematodes of man are resident in the intestine, but the filariæ and their relatives inhabit various tissues and internal organs, such as the lymph sinuses, subcutaneous connective tissue, etc. Nematode parasites of other animals, many of which are occasional or accidental in the human body, occur in practically every organ and tissue in the body — in all parts of the alimentary canal and in its walls, and in liver, lungs, kidneys, bladder, heart, blood-vessels, trachea, peritoneum, skin, eye, sinuses, etc. None, however, live as adults in the central nervous system. The surface of the body and cavities of the nose and throat of man are not the habitat of any helminth parasites except leeches and the tongue-worms; the latter are regarded as highly modified mites and are here considered with the arthropods instead of with the helminths, although they have more in common with the latter.

Life History and Modes of Infection. — The life history and mode of infection of worms varies with the habitat in the body. Every parasitic worm must have some method of gaining access to the body of its host, and must have some means for the escape of its offspring, either eggs or larvæ, from the host's body in order to continue the existence of its race. Many species utilize intermediate hosts as a means of transfer from one host to another; others have a direct life history, *i.e.*, they either develop inside the escaped egg and depend on such agencies as food and water to be transferred to a new host, *e.g.*, whipworm, ascaris, etc., or they develop into free-living larvæ which are swallowed by or burrow into a new host when opportunity offers, *e.g.*, the hookworms and schistosomes.

Most of the intestinal parasites enter their host by way of the mouth, and the eggs escape with the feces. Many species enter as larvæ in the tissues of an intermediate host which is eaten by the final host. Of such a nature are most of the tapeworms, many flukes, and some nematodes, *e.g.*, *Trichinella.* Some nematodes of the intestine, as the pinworm and whipworm, enter contaminated food or water as fully developed embryos in the eggs. Still other species, as the schistosomes, hookworms and *Strongyloides*, usually reach their destination in an indirect way by burrowing through the skin. All the intestinal worms except *Trichinella* produce eggs or larvæ which escape from the body with the feces. In *Trichinella* the larvæ encyst in the muscles and in order for them to be released the host must be eaten by another animal. Many of the worm parasites of other organs of the body also enter by way of the mouth and digestive tract, though they have various means of exit for the eggs or larvæ. The liver flukes enter and escape from the body as do ordinary intestinal parasites; the schistosomes enter by burrowing through the skin, and the eggs escape either with feces or urine; the filariæ, like blood-dwelling protozoa, enter and leave the body by the aid of blood-sucking insects; the guinea-worm enters by the mouth, and the larvæ leave through the skin. The larval tapeworms which infest man enter either by the mouth or by accidental invasion of the stomach from an adult in the intestine. Like *Trichinella* they are usually permanently sidetracked in man, except among cannibals, since they can escape only by being eaten with the tissues in which they are imbedded.

It is obvious that parasitic worms have a tremendous problem to solve in insuring the safe arrival of their offspring in the bodies of other hosts, on which the survival of the race depends. When one thinks of a fluke which can reach maturity only in the eye socket of a certain species of bird, and can not survive even in the eyes of other kinds of birds, and must, before it becomes comfortably settled down in its final habitation, go through a cycle of development in the body of a mollusc of a particular kind, one wonders how such an organism can ever survive. Likewise, when one considers the romantic experiences through which a lung fluke must go in order to live and reproduce its kind, first as a minute free-swimming protozoan-like organism, then as an asexually reproducing parasite of certain species of snails, then as a tissue-invading parasite of crabs, and finally as a human invader which must find its way from the stomach to the lungs, he would be absolutely incredulous if he were not confronted with the fact that the lung fluke not only succeeds in accomplishing this, but succeeds so well that in some places it constitutes a serious menace to the health of whole communities.

Since the vicissitudes of life for the offspring of parasitic worms are so great, it is obvious that there must be a tremendous waste of offspring which do not succeed in the struggle, and therefore a sufficiently large number of eggs or young must be produced so that the chances of survival are a little greater than the chances of destruction. The numbers necessary to accomplish this are amazing. The hookworm, *Ancylostoma duodenale*, lays, on a conservative estimate, in the neighborhood of 20,000 eggs a day, and it may do this for at least five years; the total offspring of such a worm would number over 36,000,000. If the number of hookworms in a community remains about constant, as it usually does, and the percentage of males and females is equal, the chances of a male and female hookworm gaining access to a host, and living for the full period of five years, is then 18,000,000 to one. The hookworm, however, has a comparatively simple time of it. Flukes and tapeworms, which require one or more intermediate hosts, have a more difficult problem to face, and their success can only be attributed to two special devices in their life cycles. In the first place, they have to a large extent substituted self-fertilization for cross-fertilization; they combine male and female organs of reproduction in a single individual, and do not take chances on other individuals of the opposite sex being present to render the eggs viable. In the second place, efficient egg-making machines as they are, they have found the production of sufficient eggs by one body inadequate. A tapeworm overcomes the difficulty by constantly reproducing, sometimes for years, more egg-producing segments, which are in essence new individuals, by a process of budding; some, such as *Multiceps* and *Echinococcus*, go even farther, and produce several or even many thousands of buds while in the larval stage, each of which is capable of developing into a new individual when, if ever, it reaches its final host. Flukes attain the same end in a different way. Instead of producing a sufficient number of eggs to overcome the chances of destruction through the whole cycle of development, they distribute the risk. They produce enough eggs to overcome the chances against their reaching the mollusc which serves as the first intermediate host; then, in order to overcome the odds against them in the subsequent part of the life cycle, the successful individuals reproduce parthenogenetically. Faust estimates that each offspring of a *Schistosoma japonicum* which succeeds in reaching the liver of a suitable snail gives birth, by asexual reproduction, to 10,000 progeny. Without this advantage the schistosome would probably have to produce 10,000 times as many eggs as it does.

One might reasonably ask why some worms adhere to the life cycles which they have, when so much simpler ways of reaching their hosts would seem to be available. A fluke which lives as a parasite in the intestine of a bat, for example, would seem to be very ill-advised to select a snail, on which bats do not feed, as an intermediate host, when an insect would serve so much better. Nature is in this respect strangely inconsistent, — she is a peculiar mixture of progressiveness and conservatism. In many instances, as we have seen, she has evolved the most intricate specializations both in life cycle and in structure; there are innumerable instances in the Animal Kingdom of short cuts and detours in life cycles, devised to meet newly developing conditions. On the other hand, there are some short cuts which Nature is too conservative to take. It is one of the fundamental precepts of embryology that ontogeny, *i.e.*, the development of the individual, recapitulates phylogeny, which is evolutionary development of the race. Many unnecessary phases are, however, slurred over or greatly altered, and sometimes entirely new phases are interposed to meet the exigencies of the situation, as, for example, in the case of the pupæ of insects (see p. 392). Now intermediate hosts, in which partial development occurs, are unquestionably, in most cases at least, ancestral hosts. In the case of flukes, molluscs are probably to be regarded as the hosts of the redia-like or cercaria-like ancestors of flukes. In the course of evolution these developed further until they reached the condition of modern flukes. Nature, however, has been too conservative to produce flukes in which the snail phase of the phylogeny is omitted in the ontogeny; this is apparently too radical a short cut. The result is that all flukes, regardless of their final destiny, must first be snail parasites, just as a chicken must have gills like a fish before it can have lungs like its parents. Therefore we have the irrational condition of flukes becoming first parasites of snails, then of insects and only after sojourns in these animals, parasites of bats. Undoubtedly the earliest method of transfer of flukes to their final host was by the eating of the infected snails, a method still adhered to by many flukes of snail-eating animals. In more highly specialized flukes, however, the cercariæ become impatient and leave the snail, to encyst on vegetation if the host is a vegetarian, in fishes or other animals if it is carnivorous, or, in the case of the schistosomes, to take an active instead of a passive attitude, and seek out and burrow directly into their final host.

Effects of Parasitism. — The effects produced by parasitic worms depend in part on the organs or tissues occupied, in part on the habits of the worms and in part on the poisonous qualities of their secretions or excretions, to which the susceptibility of different individuals is very variable. The effects of some kinds of worms is a much disputed point. Some investigators tend to minimize the damage done by worm parasites, especially intestinal ones, while others undoubtedly overestimate it. Improved facilities for discovering infection have demonstrated the presence of intestinal parasites in so many unsuspected cases that we are likely to incriminate them in nearly every morbid condition for which we cannot, with equal readiness, discover another cause. It cannot be doubted, however, that many of the morbid conditions really are, in part at least, produced by intestinal worms. The difference of opinion regarding the effects of worm infestations is due in part to the variable susceptibility of different races and individuals, in part to overlooking the difference in effect on normal, otherwise healthy, individuals and those handicapped by malnutrition, over-work or chronic infections such as malaria, tuberculosis, etc., and in large part to failure to take into consideration the *degree* of the infestation. Worm infections differ radically from bacterial or protozoan infections in the fact that the worms do not multiply in the body of the host, and so the infections are quantitative in nature; the severity of the infection, therefore, is not controlled almost entirely by the resistance of the host, which varies from time to time, but it depends very largely on the actual number of worms acquired. The bite of a single lightly infected mosquito may produce as severe a case of malaria as numerous bites by heavily infected mosquitoes, but the acquisition of a few hookworms, liver flukes or filariæ produces in a given individual a very different effect from the oft-repeated acquisition of large numbers of these worms. The term " infestation " instead of " infection " is frequently used to distinguish non-multiplying invaders from the multiplying ones.

In some instances even single worms, however, may cause a serious disturbance. Thus a single tapeworm such as *Diphyllobothrium latum*, which grows to a very large size, may cause severe anemia by its toxic secretions; a single gnathostome may cause a fatal perforation of the stomach wall; a single ascaris may block the bile or pancreatic duct; and a single guinea-worm creeping under the skin may cause much annoyance. In the majority of cases, however the pathogenicity of worms is proportional to the number present.

The principal ways in which helminths harm their hosts is by mechanical damage, by devouring tissues, and by toxic effects. Some large worms, like the larger tapeworms, may rob the host of enough food to have an effect at least in young growing children, but in most cases this is negligible.

The mechanical injuries are almost as numerous as the kinds of worms. Some, like the hookworms, bite the intestinal wall and cause hemorrhages, which are intensified by a secretion which prevents the blood from coagulating; some, like the lung flukes and guinea-worms, cause tissue damage and inflammation by burrowing, and may even, as in the case of *Gongylonema*, give rise to cancer-like growths; some, like ascaris, may block ducts or even cause intestinal obstruction; some, like gnathostomes and occasionally ascaris, may cause perforation of the walls of the digestive tract and consequent peritonitis; some, like the liver flukes, may choke up the bile passages of the liver; some, like Bancroft's filaria, may interfere with the normal flow of lymph and divert it into abnormal channels; some, like hydatid cysts, may interfere with the proper functioning of neighboring organs, by pressure on them due to their large size; some, like the schistosomes, may produce profound irritation of the tissues by extruding their spined eggs into them; and some, like hookworms and spiny-headed worms, open up portals of entry for bacteria. We have awakened to the importance of a " whole skin " and the danger which accompanies the piercing of it by the unclean proboscides of biting flies, bugs or other insects. We have not yet fully awakened to the importance of an uninjured mucous membrane. As has been pointed out by Shipley, the intestinal worms play a part within our bodies similar to that played by blood-sucking arthropods on our skins, except that they are *more* dangerous since, after all, only a relatively small per cent of biting insects have their proboscides soiled by organisms pathogenic to man, whereas the intestinal worms are constantly accompanied by bacteria, such as *Bacillus coli*, which are capable of becoming pathogenic if they gain access to the deeper tissues, as they are able to do through the injuries made by hookworms, whipworms, tapeworms, etc. Weinberg, for instance, found that whereas he was unable to infect unparasitized apes with typhoid bacilli, apes infested with tapeworms or whipworms readily contracted typhoid fever, the bacteria presumably gaining entrance through wounds in the mucous membrane made by the worms. The relation of intestinal worms to appendicitis is more than hypothetical, and it is probable that far more cases of appendicitis are the outcome of injury done by worms than is usually supposed.

The most serious injury from intestinal worms is undoubtedly the toxic effects of their secretions and excretions. We know that the diseases caused by most bacteria and protozoa are the result, not of the actual damage done by the parasites in devouring tissues, but of the poisonous waste products and secretions given off by these organisms. Until recently little was known about the toxic effects of worms, but that toxins were produced by them was evident from symptoms disproportionate to the mechanical injury the parasites could do, and from effects which could in no way be the direct result of mechanical injury.

Toxic substances which have an irritating action on mucous membranes, which have blood-destroying properties, or which poison the nervous system have been demonstrated in such worms as *Diphyllobothrium*, ascaris and hookworms. The general distribution of these toxic substances in the body sometimes produces profound anemia, more or less severe nervous symptoms, and a marked loss of general vitality, as shown by reduced energy, endurance, and resistance to disease. In some instances, at least, the blood-forming organs are badly poisoned; in severe hookworm infections, for example, the blood picture, with its reduced number of corpuscles and still more reduced hemoglobin, is clearly the result of interference with the normal generation of healthy blood corpuscles, and not to injury to the corpuscles already formed. Similar though often less marked anemia is characteristic of many other worm infections. Another symptom of the presence of worms in the body is a change in number and kinds of leucocytes or white blood corpuscles. An almost universal symptom, though one which is occasionally absent even in the infections in which it is most characteristic, is an increase in the number of so-called "eosinophiles," white blood corpuscles

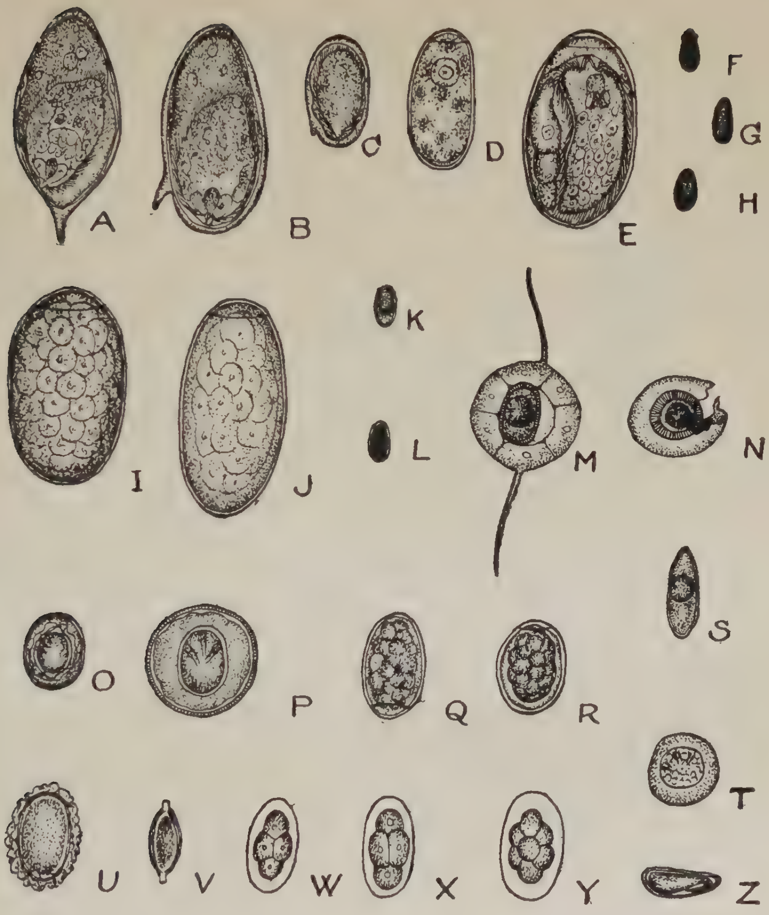

FIG. 65. Eggs of parasitic worms, drawn to scale. × 200. (After various authors.)

A, *Schistosoma hæmatobium*, voided with urine.
B, *Schistosoma mansoni*, voided with feces.
C, *Schistosoma japonicum*, voided with feces.
D, *Paragonimus westermanni*, voided with sputum.
E, *Fasciola hepatica*, voided with feces.
F, *Clonorchis sinensis*, voided with feces.
G, *Opisthorchis felineus*, voided with feces.
H, *Opisthorchis noverca*, voided with feces.
I, *Fasciolopsis buski*, voided with feces.
J, *Gastrodiscoides hominis*, voided with feces.
K, *Heterophyes heterophyes*, voided with feces.
L, *Metagonimus yokogawai*, voided with feces.
M, *Tænia saginata*, voided with feces, usually in proglottids.
N, *Tænia solium*, voided with feces, usually in proglottids.
O, *Hymenolepis nana*, voided with feces, usually in proglottids.
P, *Hymenolepis diminuta*, voided with feces, usually in proglottids.
Q, *Diphyllobothrium latum*, voided with feces.
R, *Diplogonoporus grandis*, voided with feces.
S, *Davainea madagascariensis*, voided with feces, usually in proglottids.
T, *Diplylidium caninum*, voided with feces, usually in egg balls in proglottids.
U, *Ascaris lumbricoides*, voided with feces.
V, *Trichuris trichiura*, voided with feces.
W, *Ancylostoma duodenale*, voided with feces.
X, *Necator americanus*, voided with feces.
Y, *Trichostrongylus orientalis*, voided with feces.
Z, *Enterobius vermicularis*, voided with feces.

containing granules which stain red with eosin. These cells are sometimes supposed to be for the purpose of destroying toxins in the blood just as some of the leucocytes apparently serve the purpose of capturing and destroying bacteria or other foreign cells. The mere presence of an increased number of them seems, therefore, sufficient reason for assuming the presence of toxins for them to destroy. The normal number of eosinophiles varies from 1% to 4% of the total number of leucocytes, whereas in infections with such parasites as trichina, blood flukes, echinococcus cysts, etc., the number nearly always rises to 5% or higher, and in some cases reaches over 75%.

Diagnosis. — The diagnosis of infection with various species of worms depends principally on the identification of their eggs or larvæ as found in the feces or other excretions by microscopic examination. Nearly every species of parasite has recognizably distinct characteristics of the eggs, the chief variations being in size, shape, color, thickness of shell, stage in development, appearance of the embryo if present, and presence or absence of an operculum or lid.

In many instances whole groups of worms have egg characteristics in common; for example, the eggs of flukes, except schistosomes, have an operculum at one end; those of schistosomes have spines; those of *Diphyllobothrium* also have an operculum, but the other tapeworms have eggs containing six-hooked embryos, and those of the family Tæniidæ have thick, striated inner shells; the eggs of Ascarids are thick shelled, bile stained, and with surface markings; those of whipworms and their allies are brown with an opercular plug at each end; those of oxyurids are colorless and flattened on one side; and those of the hookworms, and all their allies of the same order, have thin-shelled, unstained eggs without either opercula or surface markings. Some of the commoner worm eggs are shown in a comparative way in Fig. 65.

In cases of heavy infection it is usually possible to find the eggs in the feces or other excretions by simple microscopic examination of a smear made directly from the sample, but many light infections escape detection by this method, and various means of concentrating the eggs so that they can be more easily found have been devised. Earlier methods consisted of mixing with water, straining out the coarser particles, and then centrifuging, thus eliminating some of the lighter material. The degree of concentration thus obtained is seldom as much as 50%, however.

An extremely useful method which has come into prominence in recent years is floatation of eggs in a saturated salt solution. This method cannot be used for the eggs of flukes, or for the porous eggs of tapeworms of the family Taeniidæ, or for unfertilized Ascaris eggs, but is excellent for practically all other worm eggs. The simplest floatation method is that of Willis (1921). A tin container used for collecting fecal samples is left about $\frac{1}{6}$ to $\frac{1}{10}$ full of the feces to be examined. The feces is thoroughly stirred up with saturated salt solution until the container is brim full, and a large glass slide is then placed over it, in contact with the fluid. In about ten minutes the slide is carefully lifted off by a straight upward pull, inverted, and the surface of the fluid examined for eggs, which are seldom obscured by very much débris. A similar method is that of Kofoid and Barber, who use tumbler-shaped containers in which to stir up the feces with salt solution. They partially stir up a large sample until the mixture is of about the right consistency, force any coarse floating material under the surface with a disk of steel wool, allow to stand for about an hour, and then remove the eggs to a glass slide by removing the surface film by means of a wire loop about a half-inch in diameter.

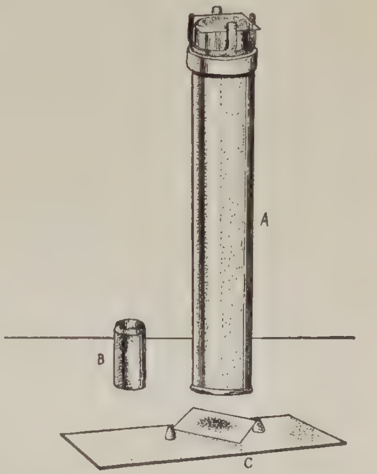

Fig. 66. Apparatus for Lane's D.C.F. method. *A*, special horned bucket containing tube with ground top and with cover; *B*, cylinder for measurement and comminution; *C*, slide ready for examination, the cover mounted on plasticine cones. (After Lane from Chandler's "Hookworm Disease.")

Recently Clayton Lane has devised an ingenious method of direct centrifugal floatation. One cc. of stool is thoroughly mixed with 18 cc. of water in a centrifuge tube, centrifuged, and the supernatant fluid poured off. The residue is then thoroughly mixed with saturated salt solution, the tube filled to the top, and covered with a special thick cover-glass. The tubes are placed in special centrifuge buckets which have four little projecting horns to prevent the cover-glass from sliding off during the centrifuging. The mixture is centrifuged for one minute at 1000 revolutions per minute, the cover-glass lifted off by a rapid upward pull, and examined as a hanging drop by mounting by the corners on two little plasticine cones on a slide. The percentage of eggs obtained and their concentration on a small area is far better than by any other method.

About 1920 Darling called attention to the importance of quantitative diagnosis of worm infections, and in recent years this has come into much prominence, especially in hookworm work. At first the average degree of infection was determined by making worm counts after treatment, but this method is so difficult and of such limited applicability that its usefulness is seriously impaired. Stoll (1923) devised a satisfactory method of estimating the number of eggs per gram in feces by diluting a measured quantity of feces in a measured quantity of N/10 sodium hydroxide solution, and counting the eggs in such a quantity that the number counted would represent 1/100 of the eggs per gram, and he also demonstrated that, within broad limits, there is a sufficient correlation between the number of eggs per gram and the number of worms harbored so that the average eggs per gram could be used as an indication of the degree or intensity of infection in a community, and the members of a community could be classified in egg-count groups in such a way as to indicate the approximate percentage with light, moderate and heavy infections. Another effective egg-count method was devised by the Caldwells (1926) in which the sample is disintegrated in antiformin and the eggs then floated in a sugar solution.

Treatment. — Treatment of the various worm infections is considered under the head of the different kinds of worms, but a few general principles should be noted here.

Drugs which are used for expelling worms are known as anthelmintics. An ideal anthelmintic is one which effectively kills or expels the particular worms for which it is used, which is not injurious to the host in the dose required, is easily administered, and is cheap. There are no anthelmintics which get a perfect score on all these counts. Not all worms are susceptible to the same drugs; there is one group, listed on p. 263, which is effective against tapeworms, and a different group which is effective against nematodes and flukes; it includes thymol, betanaphthol, chenopodium, santonin, carbon tetrachloride, and tetrachlorethylene. For some worms, especially tapeworms, careful preparation of the patient, to clean out the intestine, is necessary. Worms situated far back in the digestive tract are much harder to expel than those resident in the small intestine. Worms situated outside the intestine often have to be reached via the blood stream, and even then, as in the case of filariæ, do not respond readily to drugs; liver parasites are usually affected by absorbable drugs, such as male fern, carbon tetrachloride or gentian violet, given by mouth. Rivas has experimented with the introduction of large quantities of hot saline solution (45 to 47° C.) into the duodenum, and thinks this a safe and rapid method for the removal of all sorts of intestinal worms if properly done, but this method is by no means " fool-proof," and may be dangerous.

CHAPTER XII

THE FLUKES

General Account. — The flukes are animals of a very low order of development in some respects and of very high specialization in others. In shape they are flat and often leaflike, with the mouth at the bottom of a sucker usually at the anterior end, and in most species with a second sucker, for adhesion, on the ventral side of the body. They are all parasitic when adult and attach themselves to their hosts, either externally or internally, by means of their suckers, sometimes aided also by hooks. The development of the nervous system is of a very low grade, and the only tendency towards a brain is the presence of a small ganglion at the forward end of the body which gives off a few longitudinal nerves. Sense organs are almost lacking — there is usually no sense of sight and none of sound; in fact no sensations whatever except a meager sense of touch falls to the lot of these lowly animals. There is no blood or blood system, the result being that the digestive tract and excretory system are branched, often to a surprising extent, in order to carry food to all parts of the body and to carry waste products out from all parts. The digestive system usually has a muscular pharyngeal bulb near the mouth, and then branches into two blind pouches, the intestinal ceca; in some of the larger flukes, *e.g.*, *Fasciola hepatica*, these ceca have numerous branches and sub-branches, while in the schistosomes the ceca re-unite posteriorly to form a single stem. Only in a few aberrant species is there an anus. The excretory system consists of a complicated arrangement of branched tubules. At the ends of the ultimate fine branches are flame cells which keep up a flow of fluid towards the excretory pore. The finer branches unite in a definite manner, which varies in different groups, until finally there are only two collecting tubules which open into an excretory bladder, posteriorly placed, which in turn has an opening to the exterior by an excretory pore (Fig. 67). The type of branching of the excretory system is of value in classification but is difficult to determine in the adults; group differences are more readily determined in the living cercariæ, and are even present in the ciliated embryos or miracidia which escape from the eggs.

In the respects mentioned above the flukes are very primitive animals, but in other respects they equal or surpass any other animals in their complexity. We would have to look long to find more intricate and highly specialized reproductive systems than they possess, and their life histories are so marvelously complex as to tax our credulity. We are accustomed to think of a butterfly as having a wonderful life history in that it passes through two phases of life, the first as a caterpillar, the second as a mature butterfly, the two being separated by a third inactive phase of existence. But by comparison with the flukes this life history appears simple. Many flukes, especially those which live as internal parasites in the land animals, pass through four and sometimes even five distinct phases of existence, during some of which they are free-living, and during others may parasitize successively two or even three different hosts.

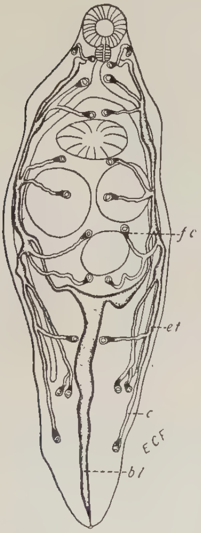

Fig. 67. Excretory system of an adult fluke (*Dicrocœlium*); *bl.*, bladder; *c*, collecting tubule; *et.*, excretory tube; *fc.*, flame cell. From "Human Helminthology" by Ernest Carroll Faust, Ph.D., Lea and Febiger, Publishers, Philadelphia.

In all flukes except those of the family Schistosomatidæ both male and female reproductive systems occur in the same individual, and occupy a large portion of the body of the animal. We are familiar with animals which appear to live almost wholly to eat; the flukes are animals which seem to live merely for reproduction. They are reproductive machines, all the other organs of their bodies being developed only to a sufficient extent to ensure the proper development and maturity of the eggs. The eggs proper, the yolk and the shell materials are produced by separate glands. In many flukes there is a minute tubule, Laurer's canal, opening dorsally, which connects with a seminal receptacle, and is believed to represent a vestigial vagina through which sperms from another individual may enter, but in some flukes Laurer's canal has no external opening and the sperms, probably often from the same individual fluke, must make their way down through the coils of the uterus, which soon becomes choked with eggs. The ovary is usually a single well-defined body. The yolk glands, or vitellaria, consist of clusters of glandular cells, usually along the sides of the body, the product of which is collected by a system of tubes and conveyed by a right and left vitelline duct to a common duct at the middle line of the body. The shell gland consists of a cluster of glandular cells around an oötype; the latter is a little chamber where the egg is assembled. It is here that oviduct, yolk duct, shell glands, seminal receptacle, Laurer's canal and uterus all come together. The egg cell has added to it yolk, sperm and shell, and is then passed along into the uterus, en route to the female genital opening. The male system consists of two or more testes for the production of the sperms; two sperm ducts which meet to form a vas deferens, usually with an enlargement, the seminal vesicle, for the storage of sperms; a cluster of prostate glands; and a retractile muscular organ or "cirrus" which serves as a copulatory organ. The seminal vesicle, prostate glands and cirrus are usually enclosed in a cirrus sac. All of these complex sexual organs in a single animal which may be no larger than the head of a pin!

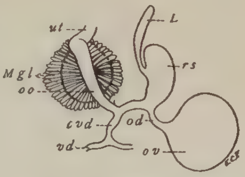

FIG. 68. Meeting place of various egg constitutents near oötype in female reproductive system of a fluke; *c v d*, common vitelline duct; *L c*, Laurer's canal; *M gl*, Mehlis or shell glands; *od* oviduct; *o o*, oötype; *ov*, ovary; *ut*, uterus; *v.d*, vitelline duct. From "Human Helminthology" by Ernest Carroll Faust, Ph.D., Lea and Febiger, Publishers, Philadelphia.

Life History. — The flukes are divisible into two subclasses, the Monogenea, which are parasitic externally or in the bladder or respiratory tubes of aquatic animals, and in which there is a simple and direct development of the eggs into adult flukes, and the Digenea, which are internal parasites and have very complicated life cycles, involving both alternation of generations and alternation of hosts. It is only with the latter that we have to deal here.

In the digenetic flukes the adult, or marita, usually lives in some part of the body of a vertebrate animal, and produces eggs which escape with the feces, urine or sputum, according to the habitat in the body. In most flukes the eggs are produced by tens of thousands, and the coiled uterus has a constant stream of many hundreds of eggs passing through it, but in the schistosomes there are only a few eggs in the uterus at a time, and production is at a slower rate, though possibly extended over a longer time.

Either before or after the eggs have escaped from the host they develop within them ciliated embryos which hatch, usually in water but sometimes in the intestine of snails which have swallowed them, by popping off the operculum of the eggs. The liberated embryos are free-swimming protozoön-like animals; they are covered by a ciliated epithelium of relatively few large flat cells, and have a short sac-like gut, a pair of secretory glands, one or more pairs of flame cells and excretory tubules, and a cluster of germ cells which are destined to give rise, parthenogenetically, to a new generation of organisms. Many miracidia have eye spots, but some are blind. The miracidia do not feed, and die in a few hours if they do not succeed in finding a proper snail host.

The miracidia (Fig. 69*A*) swim in a characteristic spirally-rotating manner, in quest of a snail of the particular species which is to serve as an intermediate host. When they come near such a snail they become greatly excited and make a head-long dash for the snail, although they ignore other kinds of snails. They attach themselves to the soft parts of the snail by the secretion of their glands and proceed to bore or digest their way into the tissues. Some miracidia, *e.g.*, those of *Clonorchis* and *Dicrocœlium*, appear not to hatch in water, but only after the eggs have been eaten by the proper snails. It is obvious that only a very small percentage of the embryos are likely to survive the double risk of not reaching water and, if safely in water, of not reaching a suitable snail in which to develop. However, once safely within the tissues of the snail the young fluke enters upon the second phase of its existence, during which it reproduces to make up for the enormous mortality encountered by its sisters during the adventurous journey from vertebrate host to snail, and to insure the survival of at least a few individuals on the equally perilous journey from snail to vertebrate, which has subsequently to be undertaken. Having arrived in the tissues of its particular kind of snail, it bores its way to the lymph spaces in the liver at the apical end of the snail and there proceeds with its development. It changes in form to an irregular-shaped sac-like or filamentous body called a sporocyst (Fig. 69*B*), which absorbs nourishment and excretes waste products through its body wall, and devotes all its energies to the development of its progeny out of the germ cells, the body cavity serving as a brood chamber. It is now a mature parthenogenetically reproducing individual, or parthenita, of the first generation, but there is usually one, and sometimes two or three, more generations of parthenitæ before the larvæ which are to grow into sexually-reproducing adults, or maritæ, are finally developed.

In the schistosomes and others of the suborder Strigeata, the offspring of the sporocysts develop into a second generation of sporocysts, but in most flukes they grow into organisms of a new type, the rediæ, constituting the second generation of parthenitæ. The redia (Fig. 69*C*) possesses a pharynx and simple sac-like gut, an excretory system of flame cells and tubules, and, in the posterior part of its body, more germinal epithelium for the production of more parthenogenetic eggs. Most rediæ have a birth-pore for the escape of their offspring when they develop, and many have a pair of blunt appendages on the sides of the body. When the rediæ are nearly mature they burst the wall of the mother sporocyst and begin an independent life in the snail's liver.

The progeny of the rediæ may be a second generation of rediæ, and even a third generation of them may be produced, but more frequently the rediæ produce offspring of an entirely different type, the cercariæ,

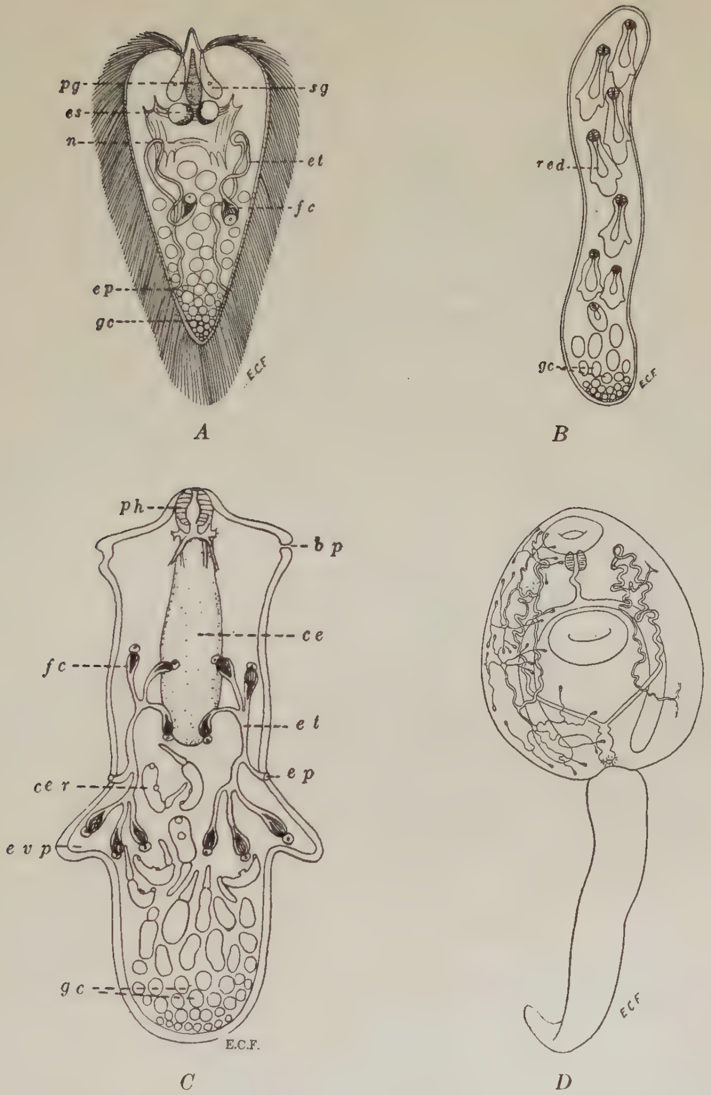

FIG. 69. Stages in life cycle of a fluke. *A*. Miracidium; *e p*, excretory pore; *e s*, eye spot; *e t*, excretory tube; *f c*, flame cell; *g c*, germ cells; *n*, nervous system; *p g*, primitive gut; *s g*, secretory glands. *B*. Sporocyst; *g c*, germ cells; *red*, developing rediæ. *C*. redia; *b p*, birth pore; *c e*, primitive gut; *cer*, developing cercariæ; *e p*, excretory pore; *e t*, excretory tube; *e v p*, evaginate appendages; *f c*, flame cell; *g c*, germ cells; *ph*, pharynx. *D*. Cercaria, showing digestive and excretory systems, but not glands. Note oral and ventral suckers, pharynx and intestinal ceca, and excretory system more complex than in redia, with posterior bladder and pore. From "Human Helminthology" by Ernest Carroll Faust, Ph.D., Lea and Febiger, Publishers, Philadelphia.

which do not become parthenogenetic adults in the snail host, but remain larvæ which, in order to complete their development, must reach, directly or indirectly, the final vertebrate host in which the sexually mature form is developed. The cercariæ (Fig. 69*D*) have a structure much more like that of the adults. The digestive system has a pharynx and a pair of intestinal ceca, there is a more complicated excretory system, and the body is provided with suckers and a tail. Nearly all cercariæ have a number of pairs of single-celled cephalic glands which open near the oral sucker, and which secrete a tissue-dissolving substance enabling them to penetrate the tissues of the final host (in the case of schistosomes), or a second intermediate host (in the case of *Clonorchis*, *Paragonimus*, etc.). In some species, such as *Fasciola* and *Fasciolopsis*, these glands apparently do not function. Most cercariæ, except those of schistosomes, also have laterally-placed glands which produce a viscous substance that " sets " as a cyst wall around the cercaria after it has lost its tail. This encysted, tailless organism is called a metacercaria. The cercariæ may encyst on vegetation after leaving the snail, *e.g.*, *Fasciolopsis* and amphistosomes, or they may encyst after penetrating a second intermediate host, *e.g.*, *Clonorchis* and *Paragonimus*, or, if the snail is eaten by the final host, they may encyst in the snail or even in the body of its parthenogenetic mother. Thus these two types of secretory glands (cephalic and cystogenous) serve either separately or in coöperation in terminating the free life of the cercaria. From this time to sexual maturity the organisms are known as adolescariæ. The cercariæ of different groups of flukes differ widely in form and structure; up to the present time only a small number of the described cercariæ have been correlated with the adult flukes to which they give rise. It is a wise cercaria that knows its own father. Various classifications of cercariæ have been devised, but until more is known about their excretory systems and their life cycles many of them cannot be fitted into any natural classification. Some of the types, on the other hand, form natural groups and can be homologized with natural groups of adults. The suborder Strigeata, for instance, all have forked-tailed cercariæ which develop directly from elongated tubular sporocysts, and actively penetrate the skin of their final hosts. One group of these, without a pharynx (Fig. 70*A*), develops into flukes of the family Schistosomatidæ, while another, with a pharynx, develops into flukes of the family Strigeidæ. The gasterostomes, too, have cercariæ with fork-like branches of the body which develop from elongate sporocysts. The cercariæ of amphistomes (Fig. 70*B*) are recognizable by the large posterior sucker, while those of monostomes (Fig. 70*C*) have no ventral sucker. The cercariæ of distomes vary greatly, and many of the groups are recognizable;

thus those of echinostomes (Fig. 70*D*) have a crown of hooks as in the adults; those of the Opisthorchidæ and Heterophyidæ have large fluted tails (lophocercous), and the latter have a spiny armature around the mouth (Fig. 70*E*); others have very small conical tails (microcercous) (Fig. 70*F*), but their relationships are unknown except in the case of *Paragonimus*; others (cystocercous) have large tails into a cavity of which the body can be withdrawn, but the adults have not been determined; others have a stylet or boring spine (Fig. 70*F*) in the oral sucker by means of which some, at least, bore into insect larvæ, such as larvæ of mosquitoes and dragonflies, and reach maturity in birds, bats, etc.; and still others, under the name *Cercariæum* (Fig. 70*G*), have no tails, encyst in their mollusc hosts, and reach maturity in fish and water-birds.

The manner in which the cercariæ accomplish the transfer from snail to final host varies greatly. The cercariæ of schistosomes are self-reliant, and actively seek the final host and bore into it when found, but most cercariæ depend on the host to pick them up. In flukes like the Fasciolidæ, amphistomes, etc., which reach maturity in herbivorous animals, the cercariæen cyst on vegetation in the water, and patiently wait to be eaten by the final host. In flukes like the Opisthorchidæ and *Paragonimus*, which mature in carnivorous hosts, the cercariæ penetrate into the tissues of fish, crabs, etc., where they encyst and await salvation by the second intermediate host being eaten by the final one. It is for this reason that many human fluke infections are prevalent only in the Orient, where fish or crabs are eaten without

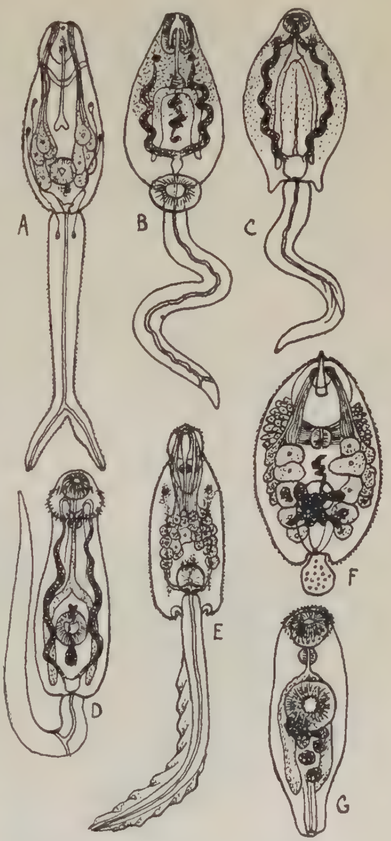

Fig. 70. Some types of Cercariæ. *A*, furcocercous, (*Schistosoma japonicum*); *B*, amphistome; *C*, monostome; *D*, echinostome; *E*, lophocercous (*Metagonimus yokogawai*); *F*, microcercous, with oral stylet (*Paragonimus westermanni*); *G*, tailless cercaria (Cercariæum). Not drawn to scale. *A*, *E* and *F* adapted from Faust, others from Cort.

thorough cooking. Some of the flukes of insectivorous animals reach their final destination by encystment of the cercariæ in insect larvæ.

The skin-penetrating cercariæ of schistosomes are carried to their final destination in the mesenteric blood-vessels by the blood stream, but encysted cercariæ always enter by way of the mouth. Their cyst walls are digested away in the stomach, and the young liberated adolescariæ migrate to the particular parts of the body of the host in which they are to mature.

The commoner types of life cycles of flukes can be seen in graphic form in the following diagram, copied from Leiper:

Host	Transition	Intermediate Host		Transition	Host
Egg	Miracidium (or ciliated embryo)	Sporocyst Sporocyst ...... Daughter Sporocyst Sporocyst ...... Rediæ Sporocyst ...... Rediæ, Daughter Rediæ	Cercariæ	Encysted in mollusc in crustacean in insect in fish on vegetation Free-swimming	Adult

Classification. — The classification of flukes is still in an uncertain state. In the first half of the 19th century only a few genera and species were recognized, and the vast majority of known flukes were placed in the genus *Distoma.* As knowledge of these worms increased, and more new forms were discovered, until now several thousands of species have been described, the genera were gradually raised to the rank of families and finally orders and suborders, while the genera which were meanwhile erected became families and were still further subdivided. Practically all of the families which were recognized as such ten or fifteen years ago have now become superfamilies. Since very few representatives of each superfamily occur as human parasites, it is unnecessary to take these into consideration here. In the past, classification of flukes has been based almost entirely on adaptive external characters and on the reproductive organs, but Faust and others have called attention to the usefulness of the excretory system, which has a constancy in fundamental pattern throughout the life cycle. It is too complicated and too difficult to study in adult flukes to be of much value, but a study of it in the miracidia and cercaria stages, in living specimens of which it is usually fairly easily seen, serves as a better guide to relationships of major groups than do such structures as suckers or even reproductive organs, since these may vary greatly in obviously related genera. In other words, taking into consideration the entire life cycle provides us with a natural

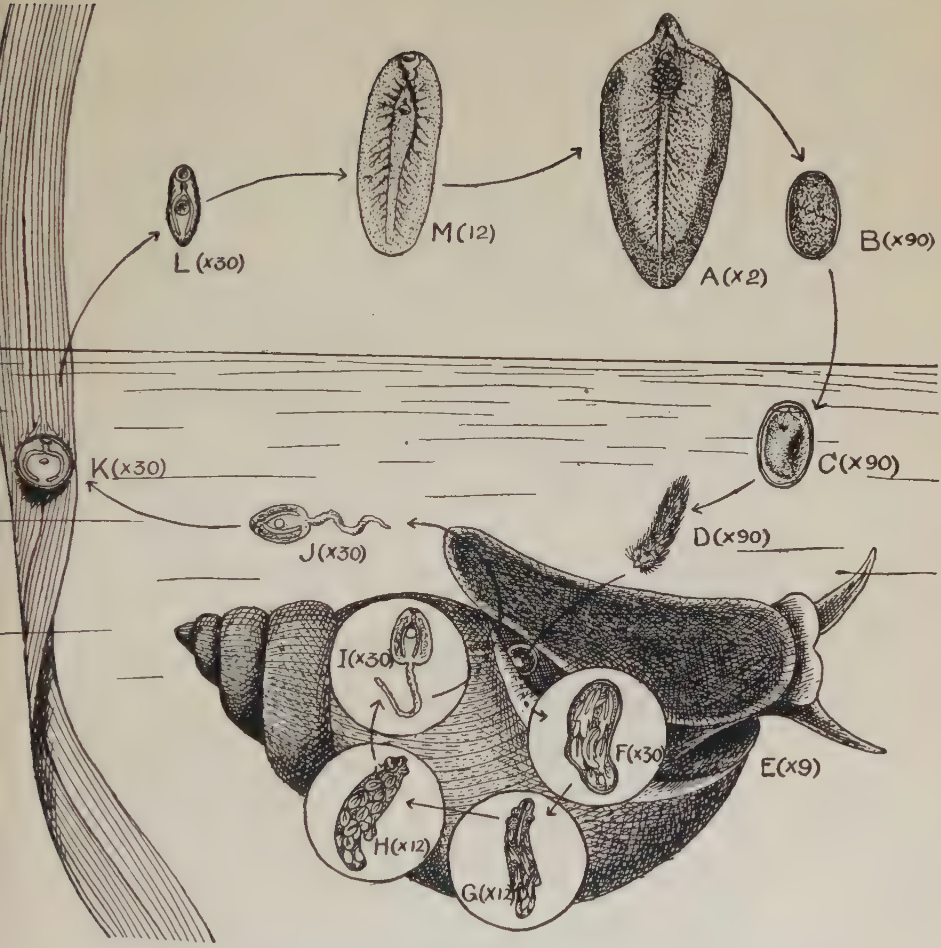

FIG. 71. Life history of liver fluke, *Fasciola hepatica;* *A*, adult in liver of sheep; *B*, freshly passed egg; *C*, egg with developed embryo, ready to hatch in water; *D*, ciliated-embryo in water, about to enter pulmonary chamber of snail (*E*); *F*, sporocyst containing rediæ; *G*, redia containing daughter rediæ; *H*, redia of 2nd generation containing cercariæ; *I*, cercaria; *J*, same, having emerged from snail into water; *K*, cercaria encysted on blade of grass; *L*, cercaria liberated from cyst after ingestion by sheep; *M*, young fluke developing in liver of sheep.

rather than an artificial classification, which is always the aim in biology, and it makes possible the recognition of characteristics of the human parasites in the various stages of development, and their consequent differentiation from the many other forms which might be encountered and confused with them.

The following table gives a synopsis of the principal major groups of flukes, following the arrangement adopted by Faust (1929).

- *I. Subclass Monogenea.* — External or semi-external parasites of aquatic animals; without parthenogenetic generations in the life cycle; with powerfully developed posterior suckers and usually anchoring hooks; excretory pores double, anterior in position.
- *II. Subclass Digenea.* — Internal parasites; parthenogenetic generations interposed in the life cycle, always in molluscs; one or two suckers for attachment; excretory pore single in maritæ, posterior in position.
  - 1. *Order Gasterostomata.* — Mouth on midventral surface; intestine a simple sac; miracidia with 2 pairs of flame cells; in aquatic animals.
  - 2. *Order Prosostomata.* — Mouth at or near anterior end, surrounded by oral sucker.
    - (1) *Suborder Aspidocotylea.* — Oral sucker absent or poorly developed in adults; ventral adhesive organ a large sucking disk or series of small suckers; intestine a simple sac; miracidia with 3 pairs of flame cells. None in man.
    - (2) *Suborder Monostomata.* — No ventral sucker; miracidium with 1 pair of flame cells. Common in birds and reptiles and occasionally in mammals, but none in man.
    - (3) *Suborder Strigeata.* — Oral sucker and one or more ventral suckers usually present; cercaria with forked tail; miracidia with 2 pairs of flame cells. Includes (1) "holostomes" which have the body divided into a flattened or cap-shaped anterior portion carrying the organs of attachment, and a more or less cylindrical posterior portion containing most of the reproductive organs, and (2), in a separate superfamily, the schistosomes, which are distinguished from all other flukes by having separate males and females living in close association, and inhabiting the blood-vessels of their hosts. These have in the past been included with the Distomata, but the life history and characteristics of the excretory system ally them with the Strigeata.
    - (4) *Suborder Amphistomata.* — Ventral sucker large and posterior in position, and often a ventral pouch or disk also present; miracidia with 1 pair of flame cells. Includes several intestinal flukes found in man.
    - (5) *Suborder Distomata.* — Oral and ventral suckers present, the latter anterior to most of the reproductive organs. Miracidia with 1 pair of flame cells. The majority of the flukes found in man belong here.

The flukes which infest man may be divided for convenience into four groups, (1) the blood flukes or schistosomes, (2) the lung flukes, (3) the liver flukes, and (4) the intestinal flukes. Over 30 different species have been recorded as human parasites, but only ten of these are common enough to be more than medical curiosities.

Control. — In all cases freshwater snails serve as intermediate hosts for the flukes which infest man and domestic animals and, except in rare instances where temporary infection comes from swallowing living adult flukes, infection always results either from active penetration of the body by the cercariæ (schistosomes) or by ingestion of the cercariæ with food or water. Knowledge of the life cycle suggests various ways in which infection might be prevented. In the first place, infection of the snails which serve as intermediate hosts could be prevented by care in preventing the excreta (feces, urine or sputum, as the case may be) from getting access to water where the snails live. Under conditions in many countries where fluke infections are endemic this is not as simple as it sounds, and in the case of the majority of the human flukes, other than the schistosomes, would be impossible because of the domestic and wild animals which serve as hosts as well as man. In the second place, infection might be controlled by preventing access of the cercaria to the human body. In the case of schistosomes this would involve prevention of bathing or wading in water containing the cercariæ, and either chlorination of water used for drinking, or storage for at least 48 hours, to insure the death of any cercariæ which might be in it; these methods have not proved successful except in special instances. In the case of flukes like *Gastrodiscoides* and *Fasciolopsis*, the cercariæ of which encyst on vegetation, avoidance of uncooked water vegetation as food would be sufficient. In the case of flukes like *Clonorchis* and *Paragonimus*, the cercariæ of which encyst in fish or crabs, cooking of such animals before eating would suffice, but it is no easy matter to change the age-old food habits of primitive peoples. In most cases, therefore, the most feasible control method is the destruction of the snails which serve as intermediate hosts. Some of them can be destroyed by desiccation, a method adopted with some success in the use of alternate canal systems in Egypt. Ducks have also been shown to be useful in the elimination of snails from some types of pools and streams.

Destruction of snails by the use of chemical substances is in many cases possible, and offers valuable possibilities. Liver flukes of cattle and sheep do not occur in salty pastures, and a liberal use of salt can, under very special conditions, be used to advantage. The writer (Chandler, 1918) found that all species of snails are destroyed by very high dilutions of copper salts. In experiments on a number of snails of six different families, including members of all the families of which species are known to act as intermediate hosts for pathogenic flukes, it was demonstrated that copper sulphate in proportions of one part in from 500,000 to 2,000,000 parts of water destroys the snails in all cases within 48 hours and often much sooner. Subsequently Khalil (1924) confirmed this work in Egypt in the case of intermediate hosts of schistosomes. The more impurity there is in the water, the more copper is precipitated out in insoluble and ineffective form, but even using crude Nile water Khalil found dilutions of 1–100,000 to 1–200,000 to be reliable, and that these concentrations had no deleterious effect on the growth or germination of field crops. The soluble copper is very soon eliminated from natural waters by combination with alkalies and organic matter. Khalil (1927) succeeded in completely destroying the intermediate hosts of *Schistosoma hæmatobium* in streams in an Egyptian oasis by treating the water — from an artesian well — with copper sulphate for four days, and the snails were still absent 6 months later. From the point of view of expense, harmlessness and convenience in use, copper sulphate is preferable to any other substance which has been tried or suggested for destroying snails. In the dilute solutions which are necessary the water is not injured either for human or animal consumption, for bathing, or for agricultural purposes. It is destructive to very few other organisms in the water, except algæ. It is, however, injurious to some species of fish, especially the young, and its use may be objected to for this reason in some places where fluke diseases are prevalent, *e.g.*, in oriental countries, where fish are extensively kept in the snail-infested waters and form an important part of the native diet. The eggs of the snails are not destroyed by the copper salts and attention has been called by Cawston to the danger of introduction of eggs or young snails, to water which has been freed of snails, in mud on the feet of birds. With government aid and supervision, the work being carried out under the direction of scientifically trained men or commissions, it seems entirely possible that whole states or countries, at least in the vicinity of towns or villages, could be freed of human fluke diseases.

Schistosomes or Blood Flukes

The most important flukes parasitic in man are three species of *Schistosoma* (formerly *Bilharzia*) which live in the mesenteric blood-vessels.

The schistosomes and their allies, constituting the family Schistosomatidæ, differ quite widely from most other flukes in a number of respects, both in structure and in life cycle. Their most striking peculiarity is the separation of males from the females into separate individuals. The relation of the sexes is one of the most remarkable in nature. The mature male worm (Fig. 72) has a cylindrical appearance due to the fact that the sides of the flat body are folded over to form a ventral groove. In this groove, projecting free at each end but enclosed in the middle, is the longer and slenderer female, safe in the arms of her lord. While young the sexes live apart, but as soon as sexual maturity is attained they couple together and spend the rest of their lives in this manner.

Unlike the liver flukes, the blood flukes do not develop great numbers of eggs all at once, but instead develop them one by one and have only a few in the oviduct at any one time. Such a method of reproduction is facilitated, of course, by the constant juxtaposition of the male and female worms. The blood flukes live correspondingly much longer than the liver flukes, often persisting for many years.

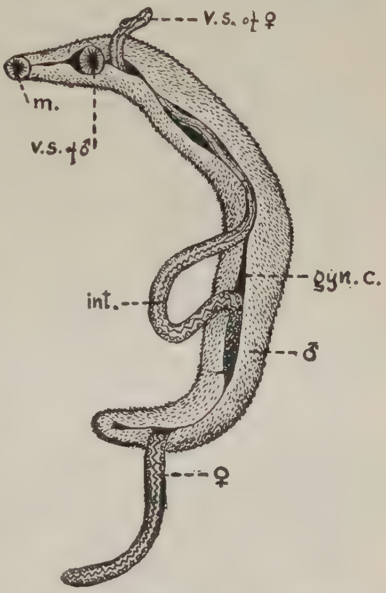

Fig. 72. Blood fluke, *Schistosoma hæmatobium;* male (♂) carrying female (♀) in ventral groove; *int.*, intestine; *gyn. c.*, gynecophoric canal or ventral groove; *m.*, mouth; *v. s.*, ventral sucker. × 8. (After Looss.)

Life Cycle. — The worms live in the branches of the mesenteric or pelvic vein, feeding primarily on blood corpuscles; from here the female repeatedly leaves her partner and makes excursions into the smallest vessels into which she can force her slender body and deposits her eggs, one at a time, in vessels next to the walls of the rectum or bladder. The eggs usually retain their position by their spines and by the blockade made by contraction of the vessels after the bodies of the parent worms have been withdrawn; they gradually work their way through the vessels into the walls of intestine or bladder and finally into the cavity of these organs, whence they escape with the feces or urine, but some of the eggs are accidentally carried to the liver, where, as in the other organs, they set up inflammations. The eggs are immature when laid, but contain fully developed miracidia by the time they escape from the body. Dilution of the feces or urine in water causes the eggs to split open within a few minutes, and the miracidium emerges; in undiluted feces or urine the eggs die in a few days. The miracidia live for only a few hours, and therefore must find a snail of the proper species within this time. When they succeed, they bore into the snail through the soft tissues, aided by the histolytic secretions of their cephalic glands, and are safely imbedded in the snail within a half-hour after the attack begins. They make their way to the liver of the snail, meanwhile transforming into tubular sporocysts which produce, out of germ cells in their bodies, a second generation of similar sporocysts instead of rediæ. These sporocysts in turn produce forked-tailed cercariæ. The latter burst the walls of the parent sporocyst and finally escape from the snail into the water in "puffs," a number at a time. Cercariæ may continue to escape from infected snails for several weeks. The cercariæ alternately swim and rest in the water for from two to three days, during which time they must reach a final host, otherwise they die. If successful they burrow through the skin, using the histolytic secretions of their cephalic glands just as the miracidia do. The natives of some parts of Africa where *S. hæmatobium* occurs realize that infection may result from bathing, but from the nature of the disease they believe that infection takes place by way of the urinary passages, and therefore employ various mechanical devices to prevent infection in this manner. The penetration of the skin requires several hours. If ingested with drinking water the cercariæ attach themselves to the mucous membranes of the mouth or throat, and similarly bore in. They burrow until they reach a blood-vessel whence they are carried, via heart, lungs, heart and aorta, to their final destination in the mesenteric veins. Those which happen

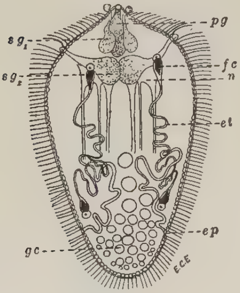

FIG. 73. Miracidium of *S. hæmatobium;* *e p*, excretory pore; *et*, excretory tube; *f c*, flame cell; *g c*, germ cells; *n*, nerve center; *p g*, primitive gut; *s* g^1, anterior salivary gland; *s* g^2, posterior salivary gland complex. × 300. From "Human Helminthology" by Ernest Carroll Faust, Ph.D., Lea and Febiger, Publishers, Philadelphia.

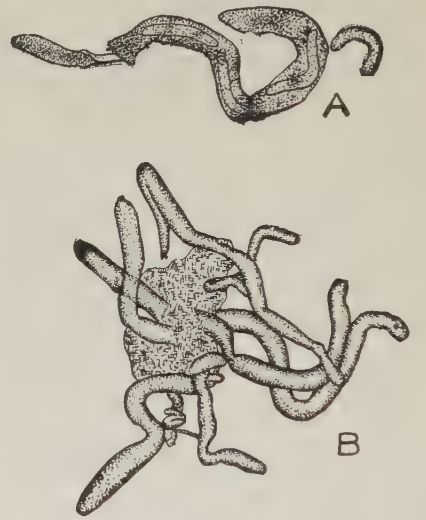

FIG. 74. Larval forms of blood flukes teased from liver of *Planorbis;* *A*, sporocyst containing daughter sporocysts; *B*, daughter sporocysts in liver tissue. (After Leiper.)

to be carried to other parts of the body are trapped, and finally die and are absorbed.

There are three species of the genus *Schistosoma*, *S. hæmatobium*, *S. mansoni* and *S. japonicum*, which habitually live in man, but these species also develop in other animals, and there are rare instances of other species maturing in man. *S. bovis* of cattle, for instance, is an accidental human parasite, and eggs of an unknown species, named *S. incognitum*, have been found in human feces. Whereas the cercariæ of human schistosomes produce little or no irritation when entering the skin, the cercariæ of other Schistosomatidæ sometimes cause severe itching and inflammation (Cort, 1928).

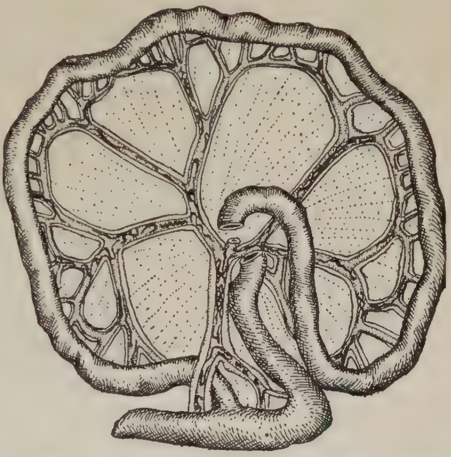

Fig. 75. Mesentery of mouse with blood-vessels infected with *Schistosoma*. (After Leiper.)

The adult schistosomes differ in details of their anatomy, and are easily identifiable by their eggs. Those of *S. hæmatobium* have a well-developed terminal spine, those of *S. mansoni* a well-developed lateral spine, and those of *S. japonicum*, which are smaller, a rather rudimentary lateral spine. *S. bovis* of cattle has spindle-shaped eggs with a spine at one end, while the eggs of *S. incognitum* are slightly flattened on the spine side, the spine being subterminal. The cercariæ of the different species vary somewhat in size, but are distinguishable with certainty only by the number and type of the cephalic glands.

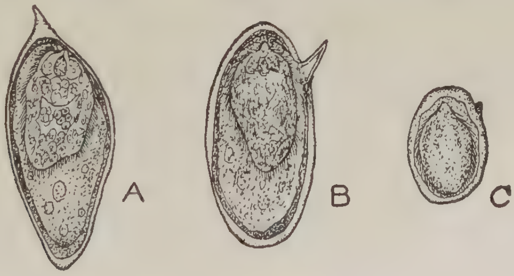

Fig. 76. Eggs of *Schistosoma; A*, terminal-spined egg of *S. hæmatobium* from urine; *B*, lateral-spined egg of *S. mansoni* from feces; *C*, egg of *S. japonicum*, with only rudiment of spine; note developed embryos in all. × about 200. (*A* and *B* after Looss, *C* after Leiper.)

Schistosoma hæmatobium. — This is probably the most important species from a pathogenic point of view. It is very common in many parts of Africa and Madagascar, and is endemic also in southwestern Asia and in some places in South Europe; it seems also to have been established in Australia. Egypt suffers especially severely — Khalil (1924) states that about 70% to 80% of the total population of Egypt are infected with schistosomes, of which *S. hæmatobium* constitutes about 90%. Christopherson (1919) said "Bilharzia (Schistosoma) probably is accountable more than anything else for the indolence of spirit, want of character, and the backward condition of development of the Egyptian peasant," a class constituting 90% of the population of the Egyptian nation. He says further, "It is almost certain that Egypt will never be able to take her proper place among the nations of consequence until she has got rid of the parasites which are poisoning her blood and consuming her energy."

The adult worms live in pairs in the pelvic branches of the portal system, and the females normally deposit their eggs in the fine vessels on the surface of the bladder, through the wall of which they work their way to be excreted with the urine, but the eggs occasionally get into other places.

The males are about 10 to 15 mm. long with flat bodies, the sides of which are rolled together to form the "gynecophoric" canal in which the female resides; in the rolled condition the body is about 1 mm. broad. The surface of the body is covered by papillæ and the suckers are armed with little spines. As in other schistosomes the digestive tract has no pharynx; the esophagus forks at the level of the ventral sucker, but the forks reunite towards the middle of the body to be continued as a single tube. There are four or five testes, lying shortly behind the large ventral sucker, and it is just behind this that the genital pore opens.

The female is cylindrical and very slender, with the cuticle covered with papillæ only at the extremities, and with a relatively small ventral sucker. The arrangement of the reproductive organs can be seen from Fig. 77.

The principal differential characters of this species are the tuberculated body and presence of 4 to 5 large testes in the male, and the position of the ovary slightly behind the middle of the body, and long uterus with 20–30 eggs in it, in the female. *S. mansoni* males also have tuberculated bodies but have 8 or 9 small testes; the females have the ovary anterior to the middle with the vitellaria occupying $\frac{3}{5}$ of the body, while the uterus contains usually only one egg. *S. japonicum* is larger; the male has most of the body smooth and has seven testes in a single column, while the female has the ovary behind the middle of the body, and has a long uterus with 50 or more eggs in it.

The intermediate hosts of *S. hæmatobium* are snails which inhabit slow-flowing canals and rivers, and quiet ponds and lagoons. In Egypt the principal snails involved are several species of *Bulinus*, while in South Africa the only important intermediate host is a snail of a related genus, *Physopsis africana*. In Portugal and Morocco a species of *Planorbis*, *P. metidjensis*, has been incriminated. The discovery, in Egypt, of the cycle of development of *S. hæmatobium* in *Bulinus* and of *S. mansoni* in *Planorbis* was made by Leiper in 1915, and finally cleared up the problem of the life history of schistosomes, which had long been a matter of dispute.

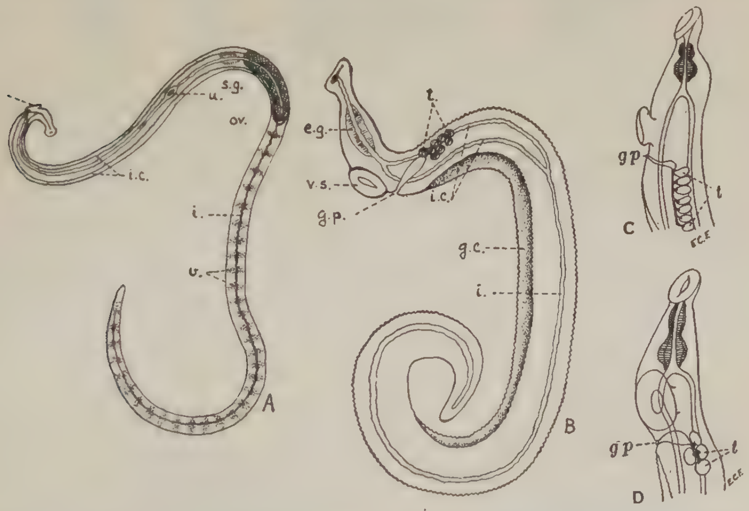

FIG. 77. Anatomy of schistosomes. *A*, female *S. mansoni;* *B*, male *S. mansoni;* *C*, anterior end of male *S. japonicum;* *D*, anterior end of male *S. hæmatobium;* *e.g.*, esophageal glands; *g.p.*, genital pore; *g.c.*, gynecophoric canal; *i.*, intestine; *i.c.*, intestinal ceca; *ov.*, ovary; *s.g.*, shell gland; *t.*, testes; *u.*, uterus; *v.*, vitellaria; *v.s.*, ventral sucker. × about 20. *A* and *B* after Manson-Bahr, *C* and *D* after Faust.

Symptoms occur first a number of weeks after infection, and consist of general toxic effects, such as headache, malaise, pain in the back and legs, and some fever. It is usually several months before the eggs begin to irritate the bladder wall and appear in the urine. At this time there is painless passage of blood at the end of micturition, and this may continue for years without other obvious symptoms, but eventually a scalding sensation appears, especially at times of micturition, which becomes more frequent, and there are dull pains in the bladder region, sometimes involving other parts of the urino-genital system. The walls of affected parts become thickened and diseased, and various deposits are formed in the bladder and urethra, and on their walls; the urethra may be entirely clogged and malignant tumors may develop in the bladder. Often pus-forming organisms invade the diseased tissues and cause abscesses or fistulas. This stage is accompanied by weakness, emaciation and intense pain in micturition. The frequency of micturition constantly increases, and often only a few drops, mostly of blood and pus, are passed each time. In severe cases the patient finally wastes away and dies. The liver and spleen may also be damaged by escaped eggs, but they are not as badly affected as in the other types of schistosomiasis. Diagnosis is usually made by finding eggs in the centrifuged urine, but in early cases in the general toxic stage, before eggs appear, use can be made of a complement fixation test devised by Fairley (1919).

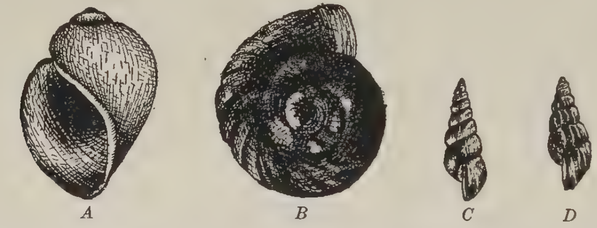

Fig. 78. Intermediate hosts of schistosomes. *A*, *Bulinus contortus*, principal host of *S. hæmatobium* in Egypt; *B*, *Planorbis boissyi*, important host of *S. mansoni* in Egypt; *C*, *Katayama nosophora*, principal host of *S. japonicum* in Japan; *D*, *Oncomelania hupensis*, principal host of *S. japonicum* in China. All × 2. (*A* and *B* after Leiper, *C* and *D* after Annandale in Faust and Meleney.)

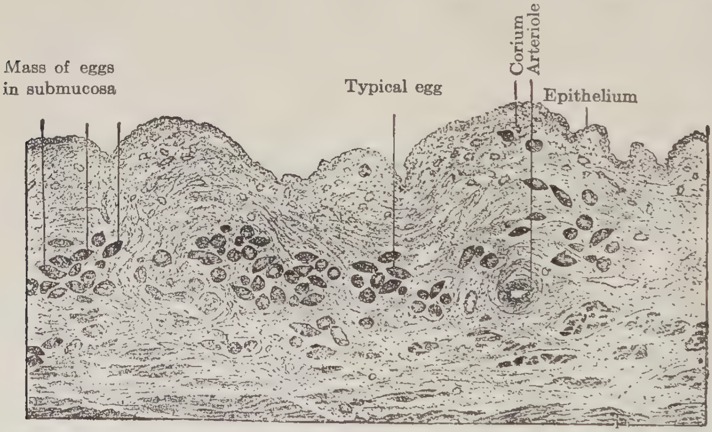

Fig. 79. Section of wall of bladder showing eggs of *S. hæmatobium*. After Brumpt.

Treatment and Prevention. — Thanks to investigations by McDonagh and Christopherson (1918–1919), we have in tartar emetic (and related antimony compounds) a drug which has a specific action on both the adult worms and the eggs. After a few intravenous injections of this drug the patient, unless the urinary tract is already profoundly injured, rapidly improves, and if the injections are not stopped too soon, permanent cure results. The eggs become fewer and fewer in the urine; those passed are shrivelled and blackened and do not hatch, and are found to contain dead and disintegrating or undeveloped miracidia. This is, of course, valuable from the standpoint of the spread of the infection. In favorable cases the eggs may cease to appear in 10 to 15 days, but in severe cases dead eggs are passed intermittently long after the parent worms are dead. Emetin has also been advocated for treatment of schistosomiasis, but in human infections, at least, it is not as effective and is more harmful to the patient. The injections of tartar emetic must be continued until no more viable eggs can be found. In advanced cases where the urinary organs have been severely damaged, surgical treatment may also be necessary.

The means of prevention must be along the lines indicated on p. 223. So far as infection from drinking-water is concerned, prevention depends on filtering, or more often impounding the water for a time sufficient to allow the cercariæ to die. Cairo, for example, where 10,000 children are said to become infected annually, obtains its water supply from the Nile, part of it being unfiltered; this water is well supplied with schistosome cercariæ from water turned back into the river from irrigation canals above the city. By impounding this water in reservoirs for 48 hours before using, the danger can be avoided. Chlorination, in the dosage commonly used for bacterial purification, has also been found to be very effective against schistosome cercariæ, killing them in a few minutes. Infection from canals, streams and ponds can only be prevented by destroying the snails inhabiting them by the methods suggested on p. 223, or by the much more difficult project of protecting such water from pollution.

Schistosoma mansoni. — This species was for a long time confused with *S. hæmatobium*, since both species occur together in Egypt, and no differences had been observed other than in the eggs. The eggs of *S. mansoni* (Fig. 76*B*) are provided with a lateral instead of a terminal spine, and are voided in the digestive tract and its appendages, whence they are liberated with the feces, instead of making an exit from the body by way of the urinary organs. By experimental infections of mice Leiper (1915) showed that cercariæ from the snail *Planorbis boissyi* (Fig. 66*B*) developed into worms somewhat smaller than those from the species of *Bulinus*, with certain distinct differences in anatomy. The cercariæ from *Planorbis* produced only lateral-spined eggs which were voided with the feces, thus showing that *S. mansoni* was really a distinct species and not merely an abnormal type of *S. hæmatobium.* This parasite occurs in common with the latter species in many parts of Africa and is also common in the West Indies, Venezuela and other parts of tropical America, where it is the only species of schistosome present. It is not unlikely that it was introduced from Africa in the slave days.

S. mansoni resembles *S. hæmatobium* quite closely in general appearance, but is slightly smaller and differs in the anatomical details noted on p. 228. The adults live in the mesenteric veins and deposit their eggs in the fine vessels of the intestinal walls, through which they gradually work their way, to be excreted with the feces.

The intermediate hosts of *S. mansoni* are in nearly all cases species of *Planorbis.* This is a very large genus of flatly-coiled fresh-water snails found in weedy ponds and streams all over the world, but fortunately not all the species seem to be able to function as intermediate hosts. In Egypt and Sudan Leiper showed *P. boissyi* (Fig. 78*B*) to be the species mainly concerned, while in South Africa Cawston has incriminated *P. pfeifferi* and also *Physopsis africana,* the latter serving as a host for both this species and *S. hæmatobium.* The intermediate host in Venezuela is *Planorbis guadeloupensis;* in the West Indies, this species and *P. antiguensis;* and in the Guianas and Brazil, *P. olivaceus* and *P. centrimetralis.* Many species of *Planorbis* occur in North America, but whether failure of the schistosomes to become established there is due to inability of these species to function as intermediate hosts, or because of fewer opportunities for transfers between snails and human beings, is uncertain.

The toxic symptoms during early stages of infection with this worm are similar to those in the case of other schistosome infections, but the later course of the disease differs from *S. hæmatobium* infection in that the intestine instead of the urino-genital system is affected. Several weeks after infection diarrhea and dysenteric symptoms develop, consisting of abdominal pain and passage of blood-stained mucus containing eggs. Usually there is a prolapse of the rectum; the walls of the small intestine, and later of the large intestine, become massively thickened and inflamed; and abscesses develop. Later papillomatous growths develop all along the intestine and fibrous constrictions appear with polyp-like growths around the anus, and there are frequently fistulas. The spleen usually enlarges, and the liver is also affected by eggs which escape to it, causing small local abscesses and finally cirrhosis. A positive diagnosis can be made by finding the eggs in the feces, but the clinical picture together with a high eosinophilia and a positive complement fixation test leaves little doubt of the nature of the infection.

Treatment and control are the same as in the case of *S. hæmatobium*, except that greater care in the use of tartar emetic is necessary on account of the frequent severe damage to the liver. The African green monkey, *Cercopithecus sabæus*, is a reservoir host, and complicates prevention by sanitary measures.

Schistosoma japonicum. — This species of schistosome is endemic in parts of Japan, China, Formosa and the Philippines, but the endemic areas are very localized except in China, where the entire Yangtse river basin, much of the seacoast, and parts of Yunnan are more or less infected. Faust estimates that about 10% of 100,000,000 people inhabiting these areas suffer from the infection.

The male worms are about 12 to 20 mm. long with a diameter of about 0.5 mm., while the females are up to 26 mm. in length. Unlike the other species the cuticle of the male, except in the gynecophoric groove, is smooth. Other anatomical characteristics are noted on p. 228.

This worm is by no means confined to man, but infects cats, dogs, cattle, horses and pigs among domestic animals, and also field mice; many laboratory animals are susceptible.

In Japan, where domestic animals are abundant, these serve as important reservoir hosts and account for the very heavy infection in certain local areas in that country. In China, on the other hand, work animals are few, and of these the water buffalos are immune and the native dogs stay away from water, so man is the only important host.

The adult worms live in essentially the same manner as *S. mansoni*, in the mesenteric veins, but the females do not leave the gynecophoric canal of the males when laying eggs, but merely move forward in it. The eggs are deposited in vessels very near the lumen of the intestine and easily penetrate into it. Later in the disease, when the intestinal wall becomes thickened, more difficulty is encountered, and more and more eggs are swept back, and on to the liver.

The intermediate hosts of *S. japonicum*, as demonstrated by Miyairi and Suzuki in Japan, are small operculated snails of the genus *Oncomelania*. In Japan and the coastal regions of China it is a species of the subgenus *Katayama*, *K. nosophora* (Fig. 78*C*), while in the Yangtse valley, with less pure water, it is *Oncomelania hupensis* (Fig. 78*D*); in Formosa it is *Katayama formosana*. These snails are small, 7 to 10 mm. in length, with high, spired shells. They are amphibious and live in damp places at the edges of water, and are commonly found climbing on vegetation in rice fields and along irrigation ditches and edges of ponds and streams, especially where the water or soil is enriched with humus or night-soil, for they feed on filth. They are frequently submerged with rising or disturbed water, and are carried from dirty village ditches to rice fields, where they thrive. While submerged they are attacked by the miracidia, which habitually swim near the surface of the water, unlike those of the other species. The discovery of the development of *S. japonicum* in *Katayama nosophora* in Japan by Miyairi and Suzuki (1913–1914) supplied the first definite knowledge concerning the life cycle of schistosomes, out of which grew Leiper's work on the other species in Egypt. Many important details of the biology and pathogenicity of this worm have been worked out by Faust and Meleney (1924).

The disease to which *S. japonicum* gives rise is essentially the same as in the case of *S. mansoni*. The general toxic stage comes on about four weeks after infection, and is often accompanied by nausea and diarrhea, and intense urticaria. When repeated infections occur, as is usual in endemic areas, the gut walls and mesenteries become progressively more thickened and inflamed, the spleen and liver are enlarged and the latter severely cirrhotic, the abdomen is distended with ascites, the body becomes extremely emaciated, and there is severe anemia and irregular rises in temperature. Retardation of development in youth, extreme weakness and breathlessness on exertion, pallor, and periodic diarrhea are characteristic of the chronic state of the disease. Many cases drag along for years, but the patients gradually go downhill, and if they do not succumb sooner as the result of other diseases like malaria or pneumonia, to which little resistance can be shown, they eventually die of exhaustion.

Treatment with tartar emetic is very successful except in severe infections of long standing, where the liver has been damaged beyond recovery, but on account of the extensive liver injury usually present even in moderate cases, care has to be exercised in the use of the drug.

Control presents a difficult problem even though the disease is largely confined to rice-growing districts. Since the snails serving as intermediate hosts are amphibious they cannot ordinarily be destroyed by adding copper sulphate to water, although this method might be used in rice nursery beds, and spraying of the sides of canals and ditches with a fairly strong solution might be effective. Some badly infected localities in Japan have been cleared by applying lime to the banks of ditches, but such a method would be agriculturally injurious, and only locally applicable, in China. Faust thinks that in Japan the best results would come from a campaign against the snails, whereas in China, where reservoir hosts are few and endemic areas tremendous in size, more hope lies in educating the rice farmers to conserve their night-soil long enough to kill the eggs before it becomes accessible to the snails.

Lung Flukes

A serious disease of man and animals, caused by invasion of the lungs by flukes of the genus *Paragonimus*, occurs in many parts of the Far East, including Korea, Japan, Formosa, Indo-China, Siam, Philippines, Malaya and parts of India, and also in New Guinea, Peru, Venezuela, Yucatan, and in parts of the United States. According to Faust there is no authenticated record of its occurrence in China. Human infection is limited to certain parts of the Far East where the second intermediate hosts, fresh-water crabs and crayfishes, are eaten without cooking. In some districts in Korea, Japan and Formosa 40% to 50% of the population are severely infected. Pigs and many carnivorous animals, including dogs, cats, and most if not all of the wild species of the dog, cat and weasel families, are subject to infection.

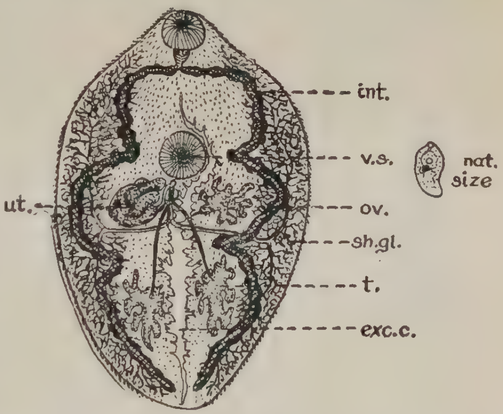

Fig. 80. Lung fluke, *Paragonimus westermanni*. Abbreviations as in Fig. 86. × about 7. (Partly after Looss, partly after Leuckart.)

The lung flukes belong to a distinct family of Distomata, the Troglotrematidæ, which Faust raises to a superfamily. There is only one genus, *Paragonimus*, affecting man and domestic animals, and opinion is divided as to whether there is more than one species. The oriental form in man, hogs and carnivores is *P. westermanni*, but the form found in pigs in the United States is regarded by Ward as constituting another species, *P. kellicotti*.

The adult flukes are reddish brown, thick, egg-shaped flukes about 8 to 12 mm. long and 4 to 6 mm. in diameter; the cuticle is clothed with minute simple or toothed spines. The arrangement of the organs can be seen from Fig. 80.

Life Cycle. — The adults live normally in the lungs where, shortly after they have arrived, the host forms cyst-like pockets around them, which rupture and liberate the eggs into the bronchial tubes, to be excreted with the sputum. These cysts are usually about the size of filberts or larger, and contain, in addition to one or two worms, infiltrated cells and numerous eggs in a rust-brown, semi-fluid mass. Many of the eggs escape into the tissues, giving it a reddish, peppered appearance, and giving rise to small tubercle-like abscesses. In some cases the worms apparently get on the wrong track in the body, and end up in such places as spleen, liver, brain, intestinal wall, eye, or muscles. Musgrave found in the Philippines that sometimes many parts of the body may be infested at once, and in one case he found over a hundred mature parasites in a muscular abscess.

The eggs of the lung fluke (Fig. 65*D*) are yellowish brown, from 80 to 118 μ in length by 48 to 60 μ in diameter, and give the sputum in which they occur a rusty-brown color; in many cases they are also found in the feces as the result of being swallowed. When immersed in water the eggs slowly develop miracidia within themselves; this process requires from four to seven weeks. The miracidia escape by popping off the operculum or cap of the egg and then swim about vigorously in search of a proper intermediate host.

The life cycle of this worm was first elucidated by Japanese parasitologists, particularly Nakagawa (1919), Kobayashi (1918–1921) and Yokogawa (1919). The miracidia were found to attack snails of the genus *Melania*, particularly, in Japan, *M. libertina*, although many other species, possibly all of them, also serve. These snails are operculated aquatic species, living attached to stones, etc., in ponds and streams. In the snails the miracidia transform into round or ellipsoidal sporocysts in which a first generation of rediæ are produced. The latter, becoming free, produce a second generation of rediæ, and these in turn produce cercariæ. The latter are 200 to 220 μ long and 70 to 80 μ broad, with a small knob like tail, a spiny cuticle (Fig. 70*F*), and an oral stylet. Several weeks are required for development in the snail.

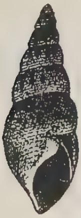

Fig. 81. *Melania libertina.* Natural size. From Faust.

After escaping from the snail the cercariæ attack fresh-water crabs or crayfish, penetrate their gills or other soft parts, and encyst. The cercariæ seem to be content with quite a variety of these crustaceans, and very likely any of the species occurring in fresh water will do.

Potamon obtusipes and *P. dehaani* are very commonly infected in Japan; the former is a coarse-shelled, chestnut-colored crab about one and a half inches in diameter, while *P. dehaani* is a slightly smaller species, grayish black or reddish in color. Both abound in shallow water of mountain streams in Japan and Formosa. In Korea another implicated crab, *Eriocheir sinensis,* inhabits rice fields near the sea and small streams inland for 40 to 50 miles, though it goes to the sea to spawn in late summer or fall. It is extensively used as food. The raw juices of the frequently infected Korean crayfish, *Astacus* (*Cambaroides*) *similis,* is used by the natives as a medicine for fever and diarrhea. *Eriocheir japonicus* of Japan is abundant in all plains rivers, and is a common article of diet throughout the country. It is a larger crab, reaching a diameter of three inches, and has large hairy claws. Another frequently infected crab is *Sesarma dehaani*, which is of medium size, dark in color with light reddish claws, and inedible.

In Venezuela another crab, *Pseudothelphusia iturbei*, has been incriminated. In the United States, since there are no fresh-water crabs, it is probable that crayfishes (*Cambarus*) serve as intermediate hosts.

The cysts containing the metacercariæ are nearly round, about 0.5 mm. or less in diameter, and have rather thick walls, formed partly from the cystogenous glands of the cercaria and partly by the crustacean host. The enclosed metacercariæ (Fig. 83) lie straight, unlike most encysted forms, and are covered with little spines.

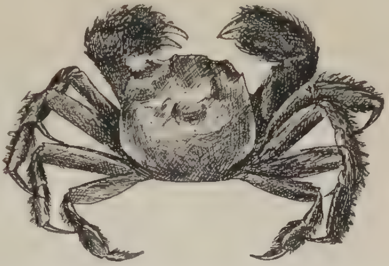

Fig. 82. A common fresh-water crab of Japan, *Eriocheir japonicus*, which serves as a host for the lung fluke. (After Yoshida.)

Infection usually results from eating the infected crabs or crayfish without cooking, but it is possible that drinking water containing cysts which have become liberated from the gills of the crustaceans may also be a source of infection, for the cysts are often easily detached, and have been found to live for some weeks in water.

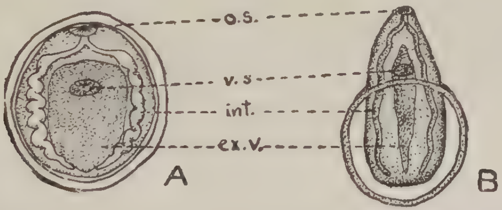

Fig. 83. *A*, encysted cercaria of human lung fluke, *Paragonimus westermanni*, from gill of crab; *B*, larva emerging from cyst. *o. s.*, oral sucker; *int.*, intestine; *ex. v.*, excretory vesicle; *v. s.*, ventral sucker. × 50. (After Yoshida.)

When the young adolescariæ are freed from their cysts in the duodenum of their final hosts, according to Yokogawa, they bore through the walls of the intestine, wander about in the abdominal cavity for some time, then go through the diaphragm to the pleural cavity, into the lungs, and finally to the bronchioles, where they remain and grow to maturity in the cysts formed by the hosts' lung tissue. Man is probably not to be considered the normal host of this worm, and it may be that the frequency with which the worms get lost and find themselves in abnormal localities may be correlated with this fact (see p. 25).

The symptoms of lung infection are similar to tuberculosis, from which, often, a differentiation can only be made by finding the eggs in the sputum. There is a cough, pains in the chest, and abundant sputum tinged with blood, or with rust-colored streaks or lumps; sometimes there are frequent hemorrhages into the lungs. When the parasites localize in other parts of the body the symptoms depend on their position; brain infections are marked by epileptic fits and other symptoms, characteristic of brain tumors, and usually in time cause death.

Treatment and Prevention. — No reliable treatment for *Paragonimus* infection has been found, though Kondo (1924) reported decrease and ultimate disappearance of bloody sputum and eggs after repeated injections of an antimony compound (stibnal). Others have reported similar results with emetin. Faust (1929), however, thinks that cures resulting from use of these drugs are doubtful, and recommends removal of patients from endemic areas when possible; recovery follows in five or six years.

Prevention of infection consists either in the destruction of the snails which act as the first intermediate host by the use of copper sulphate (see p. 223), or by abstinence from the use of raw crabs or crayfish as food, and in avoidance of water for drinking which may possibly contain detached cysts.

Liver Flukes

Fasciolidæ

There are several groups of flukes, all of the suborder Distomata, which inhabit the livers and bile ducts of man and domestic animals. Sheep, goats, and cattle are very severly damaged by flukes of the family Fasciolidæ; the most widespread and destructive species is the well-known *Fasciola hepatica*, a large, leaf-shaped fluke, 25 to 30 mm. in length, the life cycle of which is illustrated in Fig. 71. It lives in the biliary passages in the liver where it causes "liver-rot," and by interfering with the normal flow of bile, as well as by its toxic secretions, it causes much emaciation and unthriftiness especially in young animals, and is sometimes the cause of heavy losses. This species is only exceptionally parasitic in man, but occasional cases have been recorded in various parts of the world. In parts of Syria liver flukes are not infrequently eaten with the raw liver of sacrificial goats and sheep, in which case they attach themselves to the membranes of the throat causing irritation, congestion, a buzzing in the ears, difficult breathing, and other quite alarming symptoms, apparently anaphylactic in nature. Vomiting and expulsion of the worms usually gives immediate relief. It is interesting to note that a comparable temporary infection with adult flukes, *Isoparorchis trisimilitubis*, was found by the writer to be quite common in the State of Manipur in Assam, due to eating raw swim-bladders of catfish.

The eggs of *Fasciola* develop miracidia after they have been expelled from the host. The miracidia develop in snails of the genus *Lymnæa* and go through a sporocyst and two redia stages before the cercariæ are produced. The latter leave the snail and encyst on water vegetation, as is the case with all members of this family, where they remain until eaten by the final host. The cercariæ are not infective until about 12 hours after encysting. The cysts withstand short periods of drying.

A nearly related but longer worm, *F. gigantica*, replaces *F. hepatica* as a bovine parasite in Africa and parts of the Far East. Three records of human infection are known. Another related worm, *Fascioloides magna*, is common in cattle in southern United States, but has not been found in man. It habitually burrows in the liver tissue instead of remaining in the biliary ducts. One of the commonest human intestinal flukes, *Fasciolopsis buski*, belongs to the same family; it is discussed on p. 247.

Dicrocœliidæ

In many parts of the world, but particularly in Europe, herbivorous animals suffer from another liver fluke infection, caused by the so-called lancet fluke, *Dicrocœlium dendriticum* (*lanceolatum*). This is a very flat, lanceolate fluke measuring 5 to 15 mm. in length by 1.5 to 2.5 mm. in breadth. Its structure can be seen from Fig. 84. The thick-shelled, brown eggs, measuring 40 to 45 μ by 22 to 30 μ, usually contain miracidia when laid, but they do not hatch in water, and the life cycle is still unknown in spite of numerous attempts by European helminthologists to work it out. Probably the eggs hatch after ingestion by a snail, and it is very likely that the cercariæ encyst on vegetation as in the case of the Fasciolidæ. It produces effects similar to those of *Fasciola*, but less severe. Human cases are not infrequent in Europe, and many cases have recently been recorded from Tashkent in Turkestan; the possibility exists, however,

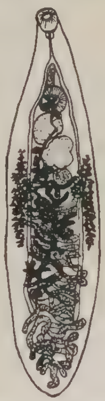

FIG. 84. *Dicrocœlium dendriticum.* Note position of two testes anterior to the smaller ovary. (After Looss.) × 5.

that some of the cases in which eggs of this parasite are found in human feces may be due to their ingestion with the livers of infected animals.

Another fluke of the same family, *Eurytrema pancreaticum*, which is shown in Fig. 85, lives in the pancreatic ducts of pigs and in the biliary ducts of cattle, water buffalos and camels in China. Its thicker body and large oral sucker suffice to distinguish it from *Dicrocœlium*. A few human cases have been recorded from South China.

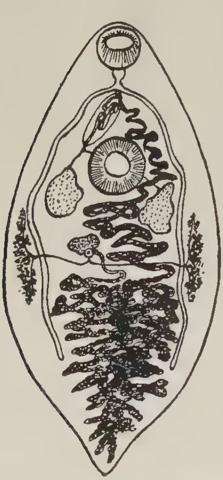

Fig. 85. *Eurytrema pancreaticum*, seen from dorsal side. × 5. Partly after Railliet.

Opisthorchidæ

The flat, elongate, semi-transparent flukes of this family occur in flesh-eating, or rather fish-eating, animals, particularly in Europe and Asia, but one species has been found in cats in the United States. The general arrangement of the organs can be seen from Figs. 86 and 91. The eggs of these flukes are very small and contain miracidia when laid, but the latter do not ordinarily hatch until eaten by a suitable snail. The cercariæ encyst in fresh-water fishes, and reach their final hosts when these are eaten.

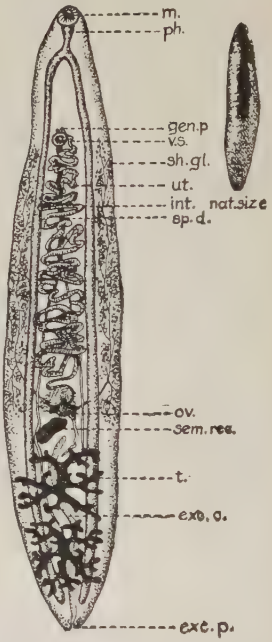

Fig. 86. The Chinese fluke, *Clonorchis sinensis*. × 3½. *m.*, mouth in oral sucker; *ph.*, pharynx; *gen. p.*, genital pores; *v. s.*, ventral sucker; *sh. gl.*, vitelline or yolk glands; *ut.*, coiled egg-filled uterus; *int.*, intestine; *sp.d.*, sperm duct; *ov.*, ovary; *sem. rec.*, seminal receptacle, where sperms for fertilizing eggs are temporarily stored; *t.*, testis; *exc.c.*, excretory canal; *exc. p.*, excretory pore. (After Stiles.)

Clonorchis sinensis.—Much the most important species from the standpoint of human disease is the Chinese liver fluke, *Clonorchis sinensis*, which is widely distributed in the Far East from Korea and Japan through China to Indo-China. It is a common parasite in cats, dogs, pigs, and various wild carnivores, as well as man. Human infection is limited to those areas where fish are eaten uncooked, which greatly limits it, for although other hosts are heavily infected over a large part of the Yangtse Valley of China, the Chinese of this region do not esteem raw fish as a delicacy, as they do in some other localities, and therefore human infection is rare. On the other hand heavy human infections are very common in certain local areas in Japan, in the vicinity of Swatow and Canton in China, and in the Red River delta in French Indo-China. In some localities 75 to 100% of the natives are infected.

The adult flukes vary from 10 to 25 mm. in length and are from 3 to 5 mm. wide, with an arrangement of organs as shown in Fig. 86. The deeply branched testes distinguish this genus from the related *Opisthorchis*, in which the testes are round or lobed. The adults live both in the small biliary ducts of the liver and also in the larger bile ducts leading to the gall bladder, often in hundreds or even thousands.

The life cycle of *Clonorchis* has been worked out in recent years by Japanese parasitologists. Kobayashi (1910) discovered that cyprinoid fishes served as second intermediate hosts, and Muto (1917) discovered the first intermediate host. This work was confirmed, and many details added, by Faust and Khaw (1927).

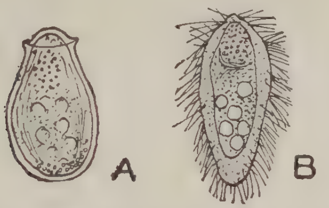

Fig. 87. Egg and ciliated embryo of Chinese fluke, *Clonorchis sinensis*. × 700. (After Katsurada.)

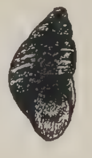

Fig. 88. *Parafossalurus striatulus*, intermediate host of *Clonorchis*. × 2. Sketched from Annandale in Faust and Khaw.

The small yellow-brown eggs, averaging 27 by 16 μ in size, are shaped like an old fashioned, carbon-filament light bulb, the operculum fitting into a thickened rim of the shell like the lid on a sugar bowl (Fig. 65*F*). The miracidia, already developed when the eggs are laid, do not hatch until the eggs are eaten by suitable snails, which are small, conical, operculate snails of the subfamily Bythiniinæ, which belong to the same family as the intermediate hosts of *Schistosoma japonicum*. The most important species is a 6-whorled, horn-colored snail, *Parafossalurus striatulus*, about 11 mm. in length, which is widely distributed in canals and ponds throughout the area where human infections occur. A few other species of this genus and of *Bythinia* have also been incriminated. It is possible that species of *Melania* may also serve in some localities.

In the snails the miracidia, which have asymmetrical internal organs, develop into rounded sporocysts which produce rediæ, without either birth-pore or foot-like procesess, and the latter give birth to the characteristic cercariæ (Fig. 89). These cercariæ attack fresh-water fishes, mainly of the family Cyprinidæ, such as various carp, grudgeon, bitterling, and the Chinese "ide" and "big-headed fish." They penetrate under the scales and into the soft parts, lose their tails, and become encysted. When the fish is subsequently eaten by a suitable host the cyst wall protects them from digestion in the stomach, and they are liberated in the small intestine. From here they explore their way into the bile duct, migrate to the biliary passages of the liver, and there grow to maturity. They may live for from 5 to 20 or more years.

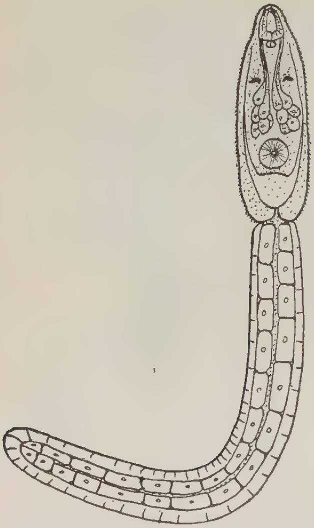

Fig. 89. Cercaria of *Clonorchis sinensis*, × 120. Adapted from Faust and Khaw.

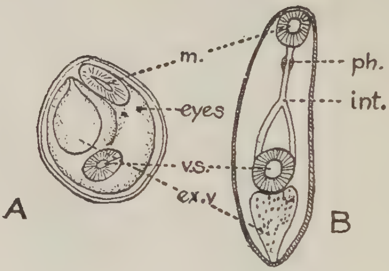

Fig. 90. Larvæ of Chinese fluke; *A*, cercaria encysted in fish; *B*, larva freed from cyst; *m.*, mouth in oral sucker; *v. s.*, ventral sucker; *ex. v.*, excretory vesicle; *ph.*, pharynx; *int.*, intestine.

Epidemiology. — It is obvious that, in order for this infection to thrive, conditions must be favorable for infection of snails by the eggs, for infection of suitable fishes by the cercariæ, and for infection of man or animal by the cysts in the fish. Observations by Faust and Khaw in infected localities show how well these conditions are fulfilled. In the Okayama district of Japan, for instance, the backdoorsteps of farm houses commonly lead down to an irrigation canal. Close to each doorstep, along the canal, is a large earthenware jar containing the night-soil of the household, and in the canals are abundant snails and cyprinoid fishes. The people are very fond of the fishes eaten raw in salads, and also use the canal water, containing viable *Clonorchis* cysts freed from dead fish, for drinking. In the mulberry-growing areas near Canton latrines are placed over fish ponds, the feces falling directly into the water or onto night-soil rafts, and much of it is consumed by the fishes, the remainder sinking to the bottom and disintegrating in the mud. Once a year the water is cleared out, the fish harvested, and the muck used for fertilizer. Suitable snails occur in the ponds and feed on the fecal material, the fish, mainly "ide" and "big-headed fish" are attacked by the cercariæ subsequently developed, and the people become infected when they eat the raw fish sliced with radishes or turnips and highly seasoned, which they do especially on feast days. Both here and in French Indo-China fish are often not eaten entirely raw, but are laid on top of a dish of steaming rice where they are heated sufficiently to remove the raw taste, but not to kill cysts in the interior of the flesh. Others merely dip the fish into hot water or broth, with similar results.

The Disease and its Treatment and Prevention. — The flukes live in the biliary passages of the liver, where they injure the epithelium of the ducts, and ingest blood. If numerous they may seriously clog the ducts. The walls of the ducts become thickened, and neighboring portions of the liver tissue may be involved, in severe cases leading to a general cirrhosis. Light infections may show no symptoms at all; more severe infections are accompanied by diarrhea, often with blood, edema, enlarged liver, and the usual symptoms of cirrhosis of the liver. The patient ultimately becomes anemic, emaciated and weak, and is ready prey for other diseases.

Treatment is more or less uncertain. Some workers have obtained good results with injections of antimony compounds, but others have failed. Faust and Khaw found that complete cures could be effected in early cases by gentian violet and related dyes given in the form of coated pills, and that even in cases of long standing a proportion of the worms could be reached by a sufficient concentration of the dye to kill them.

Prevention would be possible by modifying the methods of utilizing night-soil, either storing it undiluted or adding 10% of ammonium sulphate, to kill the eggs before snails got access to them. The snails withstand desiccation for several weeks, and cannot be destroyed by the use of copper sulphate in fish ponds on account of the susceptibility of the fish, so destruction of the snails appears impracticable. The best means of prevention, therefore, is to educate the people to the dangers inherent in the use of fresh-water fish as food, unless well cooked. Even dried and salted fish may contain viable cysts for some time. Since, however, the people like raw fish as food, and since the cost of the extra fuel required to cook it is a real economic factor, it will not be easy to do away with the habit of eating it uncooked.

Human *Clonorchis* infections never occur in places where fish is not eaten raw, even though infection is common in animals, and this is also true of other Opisthorchidæ. In parts of India, for instance, *Opisthorchis* infections are extremely common in cats and pariah dogs, yet human infections are unknown among the native Indians, who never eat raw fish.

Clonorchis infections have been found in Orientals in all parts of the world, but two factors are necessary for it to become endemically established, (1) the presence of a suitable snail to serve as an intermediate host, and (2) the habit of eating raw fish. American quarantine regulations against *Clonorchis*-infected Orientals on the Pacific Coast seem quite unnecessary, since there is no evidence that a suitable snail occurs there and, even if it did, the disease could never spread beyond small local colonies of raw-fish-eating Chinese or Japanese.

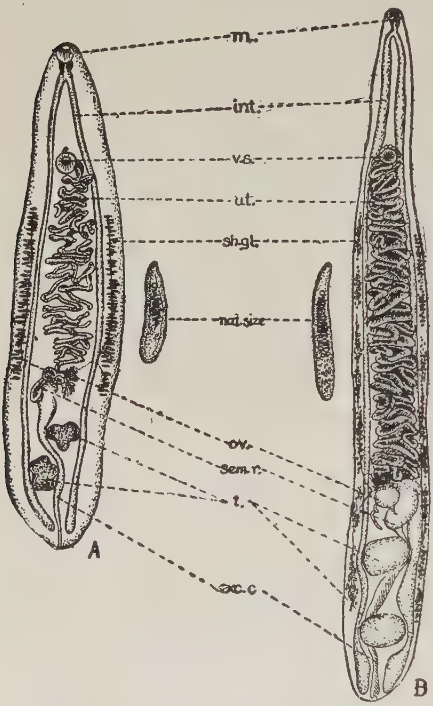

FIG. 91. *A*, cat fluke, *Opisthorchis felineus*; *B*, American cat fluke, *O. pseudofelineus*. Abbreviations as in Fig. 86. × about 5. (*A*, after Stiles and Hassall; *B*, after Stiles.)

Other Opisthorchidæ. — The related genus *Opisthorchis* contains several species of flukes similar in general appearance to *Clonorchis*, but differing in the form of the testes (see p. 241), which are parasitic in cats and dogs and related animals, and occasionally in man. One very wide-spread and common species is *Opisthorchis felineus*, found from Central and Eastern Europe to Japan. In Calcutta the writer found over 60% of the cats infected. It is about 7 to 12 mm. long and 2 to 3 mm. broad, with habits similar to *Clonorchis*. The life cycle has not been worked out, but is undoubtedly very much like that of *Clonorchis*. The eggs are more slender than those of *Clonorchis*, averaging about 30 by 11 μ. The encysted cercariæ have been found in cyprinoid fishes in Europe. Human infections are common in certain districts where the fish are eaten uncooked, as in East Prussia and in the vicinity of Tomsk, Siberia. Two other species, *O. viverrini* and *O. noverca*, the former in southeastern Asia and the latter in India, have similar habits and have also been recorded from man. *O. viverrini* occurs in about 25% of the natives of the Lao country of Northern Siam, according to stool examinations. The very elongate *O. pseudofelineus*, found in cats and coyotes in central United States, would probably also infect man if opportunity were offered. Another species, *Pseudamphistomum truncatum*, distinguished by the truncated posterior end of the body, inhabits the livers of carnivores in Siberia, and is also likely to occur in man.

The pathogenic effects, treatment and epidemiology of these infections do not differ in any way, so far as known, from those of *Clonorchis*.

Intestinal Flukes

There are many widely different kinds of flukes which inhabit the intestines of their hosts; in fact they occur in every order and suborder. Two suborders, the Amphistomata and the Distomata, include forms which are at least occasionally parasitic in the human intestine. There are no intestinal flukes which can properly be regarded as primarily parasites of man, though a few of the species are very commonly found in him, at least in certain localities; the majority of them cause rather rare, accidental infections. On account of the omnivorous and variable food habits of the human being, he is subject to a very wide range of such accidental parasites, including species properly belonging to both carnivorous and herbivorous hosts; probably no other animal except the pig can compete with man in this respect. We shall consider the following groups or species of intestinal flukes: (1) amphistomes, normally parasitic in herbivores; (2) *Fasciolopsis*, normally in pigs; (3) Heterophyidæ, normally in carnivores; and echinostomes, the human species of which probably occur normally in carnivores.

Amphistomes. — Although some kinds of amphistomes have adapted themselves to life in cold-blooded vertebrates and birds, most of them live in the stomach or intestine of herbivorous mammals, such as goats, sheep, cattle, horses, deer, camel, pigs and elephants. In some localities practically every animal of some of these kinds has colonies of amphistomes carpeting small or large areas on the walls of stomach or intestine. There is only one species which is at all frequently found in man, namely *Gastrodiscoides hominis*, a pig parasite. Human cases are by no means uncommon among the hill tribes of Assam; in one case over 750 worms were expelled. It has also been found in man in Cochin-China and in Indian immigrants in British Guiana. It is common in pigs in southern Asia, and a high percentage of these animals are infected in Bengal and Assam.

The worm inhabits the cecum and large intestine of its host, where it causes some inflammation and diarrhea. The adult worms, 5 to 7 mm. in length when preserved, have an orange-red appearance when living, due to a fine network of bright red capillary-like structures in the cuticle, against a flesh-colored background. The body is divided into two parts, — a very active, slender, conical or finger-like anterior portion which has the genital pore on its ventral side, and an almost hemispherical posterior portion, scooped out ventrally in a disk-like manner, with a sucker near its posterior border and a notch at the posterior end. Several nearly related species, in the genus *Gastrodiscus*, occur in the intestines of horses and pigs in Africa.

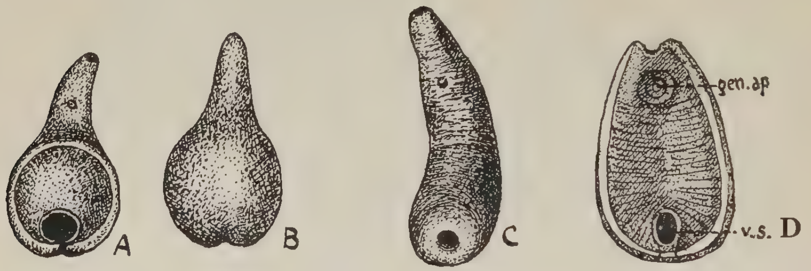

Fig. 92. Amphistome flukes. *A* and *B*, *Gastrodiscoides hominis*, ventral and dorsal views; *C*, *Paramphistomum cervi*, ventral view; *D*, *Watsonius watsoni*, ventral view. × about 4. (*A*, *B* and *C* original, *D* after Stiles and Goldberger.)

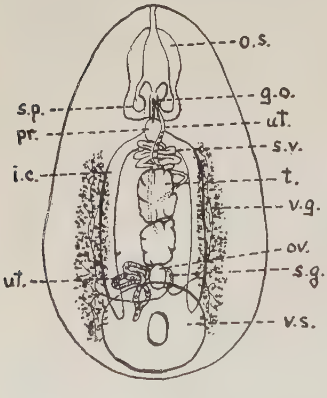

Fig. 93. Internal anatomy of *Watsonius watsoni*; *g.o.*, genital opening; *i.c.*, intestinal cecum; *o.s.*, oral sucker; *ov.*, ovary; *pr.*, prostate gland; *s.g.*, shell gland; *s.p.*, suctorial pouch; *s.v.*, seminal vesicle; *t.*, testis; *ut.*, uterus; *v.g.*, vitelline glands; *v.s.*, ventral sucker. ×6. (After Stiles and Goldberger.)

The eggs are very large, as are those of other amphistomes, somewhat narrower at the opercular pole and with the shell thickened at the opposite pole. The miracidia develop after the egg has escaped from its host, but nothing is known of the life cycle beyond this point. By analogy with other amphistomes, there is little doubt but that the cercariæ encyst on water vegetation, and that the life cycle is essentially similar to that of the Fasciolidæ.

The only other amphistome so far found in man is *Watsonius watsoni*, and this has been recorded but once, from the small intestine of an emaciated negro who died from severe dysentery in Nigeria; its normal hosts appear to be monkeys, in which the parasite has been found in Africa, Malaya and Japan. The worm when living is reddish yellow; it is a thick, pear-shaped animal, slightly concave ventrally, with a translucent gelatinous appearance. It is about 8 to 10 mm. long and 4 to 5 mm. broad. It belongs in the same family as the rather maggot-shaped amphistomes (*Paramphistomum cervi*, etc.) which are abundant in the fourth chamber of the stomach of ruminants. So far as the details are known, the life cycle of these worms is essentially like that of *Fasciola.*

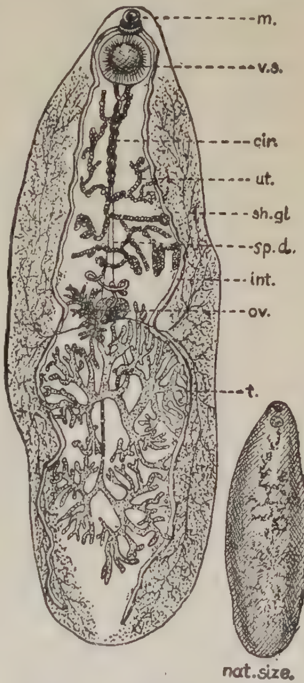

Fig. 94. *Fasciolopsis buski,* ×2½. Abbreviations as in Fig. 86. (After Odhner.)

Treatment is considered on p. 249. Since the details of the life cycle are unknown, there is little that can be said about prevention, but it can be accepted as fairly certain that avoidance of eating any uncooked water vegetables grown in water likely to have been contaminated by eggs of the worms would protect against infection.

Fasciolopsis. — Another parasite which man shares with pigs is a large fluke of the genus *Fasciolopsis,* of which there is now believed to be but one species, *F. buski.* This is a flat but rather fleshy oval fluke, creamy pink in color, which reaches a length of from 2 to 7.5 cm. When preserved it contracts and thickens, but fresh, relaxed specimens are very large and rather thin and flabby. In some ways it resembles the liver fluke (*Fasciola hepatica*) of sheep and cattle, but it has no thickened cone at the head end, and have unbranched intestinal ceca. It is widely distributed in pigs in the Far East, from Central China, throughout southeast Asia, to Assam and Bengal, and also in many of the East Indian Islands. Human infections are much more limited, but are very common in some parts of China. Occasional cases occur in various places in India, but it is only in the Manipur Valley of Assam that it is at all frequent in that country. In some villages near Shaohsing, China, according to Barlow, 100% of the people examined were found to be infected, and in that area it profoundly affects the life of between a million and a million and a half people, reducing their efficiency and causing great loss of life.

The life cycle of the worm was first worked out by Nakagawa (1921) in pigs and later in more detail by Barlow (1925) in man. The eggs are large and very variable in size, but average about 138 by 83 μ. The miracidia require several weeks to develop after they are passed by the host. The intermediate hosts are very small, flatly-coiled aquatic snails, including *Segmentina nitidella* and *S. schmackeri* in China and *S. hemisphærula* (*largeillierti*) and *Planorbis cœnosus* in Formosa. In the snails the miracidia change into sporocysts, which are peculiar in possessing a sac-like gut like a redia, but no pharynx. Two generations of rediæ are produced, the second generation of which produce large heavy-tailed cercariæ, measuring, with the tail, nearly 0.7 mm. in length. The free-swimming life is brief, occupying only time enough for the cercaria to get to the plant on which the snail is feeding. In one to three hours the cercaria has lost its tail and has encysted. The cysts are white, and about 200 μ in diameter. The whole development from infection of snails to encystment occupies about seven weeks.

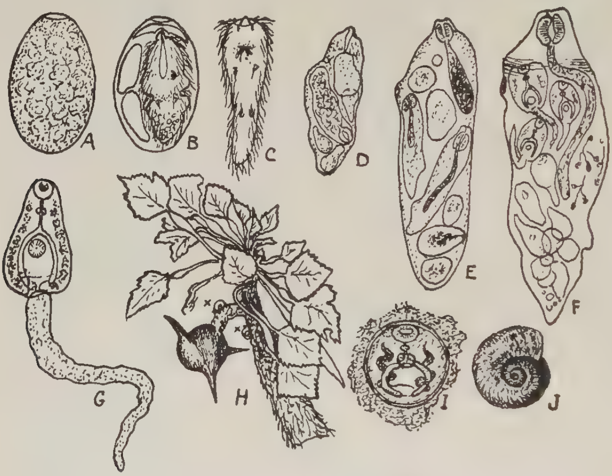

FIG. 95. Stages in life cycle of *Fasciolopsis buski*. *A*, egg as passed in feces, showing yolk balls; *B*, egg containing developed miracidium, with "mucoid plug" at anterior end and oil globules at one side; *C*, miracidium, showing eye spots; *D*, sporocyst containing developing mother rediæ; *E*, mother redia containing developing daughter rediæ; *F*, daughter redia containing developing cercariæ; *G*, cercaria; *H*, Chinese caltrop or water ling (*Trapa natans*) with snails at points marked "X"; *I*, encysted cercaria; *J*, *Planorbis schmackeri*, intermediate host. *A–D*, × 140; *E*, × 50; *F*, × 40; *G* and *I*, × 70; *H*, × $\frac{1}{5}$; *J*, × $1\frac{1}{4}$. Sketched from figures by Barlow.

In China, human infection has been traced mainly to the eating of the nuts of a water plant known as the red caltrop or red ling (*Trapa natans*). These are extensively cultivated in ponds in the endemic areas, and are fertilized by fresh night-soil thrown into the water. The little snails abound in these warm stagnant pools, and the plants are fairly alive with them, creeping over their stems and leaves. The snails, of course, become infected by hatched miracidia, and the escaped cercariæ subsequently encyst on the plants and nuts. The nuts are eaten both fresh and dried. When fresh they are kept moist, and are peeled with the teeth, during which process the cysts gain access to the mouth and are swallowed. Barlow examined nuts from typical ponds, and found from a few to over 200 cysts on each nut. Another plant carrying infection is the so-called water chestnut, *Eliocharis tuberosa*, which has tubers like Gladiolus bulbs. They are grown in flooded fields, in which the water is allowed to dry down to mud as the tubers mature. The snails move down to the tubers, and the latter frequently harbor *Fasciolopsis* cysts which reach the mouth when the luscious bulbs are peeled with the teeth and lips, and eaten. The writer (1928) traced some cases of infection in Eastern Bengal to the eating of a water nut, *Trapa bicornis*, closely related to the Chinese nut.

Fasciolopsis buski usually lives in the small intestine where it causes local inflammation, and also poisons the body by absorbed toxic products. Symptoms develop about three months after infection. According to Goddard there are three stages in the disease caused by this parasite. There is first a period of latency during which there is some asthenia and mild anemia. This is followed by a period of diarrhea, in which there is more or less intestinal disorder; there is, however, no blood in the diarrheal stools. There is always noticeable anemia, and this may be extreme. A combination of chronic diarrhea and anemia is said to be characteristically the result of *Fasciolopsis* infection in Shaohsing. Often the abdomen is protuberant in children. The third stage is characterized by increased anemia and a distressing amount of edema, which affects the abdominal cavity first, then the legs, and finally the upper portions of the body. It gives the affected parts of the body a very characteristic swollen appearance.

Treatment and Prevention. — Although the flukes are related to the tapeworms and not to nematodes, the intestinal species are more susceptible to the group of anthelmintic drugs which are effective against the nematodes. According to Barlow (1925) *Fasciolopsis buski* is easily gotten rid of by a number of different drugs, among which he includes oil of chenopodium, oil of turpentine, beta-naphthol, thymol, and carbon tetrachloride, as well as some native drugs containing areca nut. Carbon tetrachloride is considered the most efficacious drug, but beta-naphthol is recommended as the nearest to a safe remedy.

Prevention consists in educating the people of endemic areas to the danger of eating fresh-water ling, water chestnuts, or other water vegetables unless they are cooked or at least given a brief immersion in boiling water. Sterilization of night-soil would also be effective but that presents an infinitely more difficult problem.

Heterophyidæ. — The flukes of this family are extremely small, egg-shaped flukes, no larger than the head of a pin, which are normally parasitic in fish-eating animals. They have the cuticle covered with minute scale-like spines, and the genital pore opens into a retractile sucker-like structure which is either incorporated in the ventral sucker or lies to one side of it; Witenberg (1929) calls this structure a "gonotyl." The arrangement of organs can be seen from Fig. 96. The life cycle is practically the same as that of the Opisthorchidæ, and a closely related group of snails serve as intermediate hosts. The eggs are difficult to distinguish from those of *Clonorchis*; they are similar in size (20 to 35 μ by 11 to 20 μ) but they lack the mosaic marking of the shell which characterizes the eggs of the Opisthorchidæ, and the enclosed miracidium has the internal organs symmetrically arranged. The parthenitæ consist of a sporocyst and two redia generations, at least in some species, and the cercariæ, though strikingly like those of *Clonorchis*, have a special arrangement of spines around the mouth which distinguishes them. The cercariæ encyst in fresh-water fishes, which serve as vectors to the fish-eating final hosts. Development in the final host is very rapid, maturity being reached in from 7 to 10 days. All of the species seem to be remarkably versatile concerning their hosts, and can develop not only in a great variety of mammals but also in birds, although they seem to grow largest and persist longest in dogs. It is possible for many of the species of Heterophyidæ to accidentally infect man, but two species, *Metagonimus yokogawai* and *Heterophyes heterophyes*, are known to be common human parasites in certain localities.

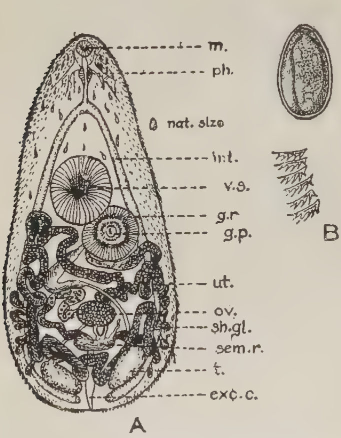

Fig. 96. *Heterophyes heterophyes*, a very small intestinal fluke of man; *A*, adult; *B* (× 350), spines from genital ring; *g. r.*, genital ring; *g. p.*, genital pores; other abbrev. as in Fig. 86. × 33. Egg shown above, × 500. (After Looss.)

Metagonimus yokogawai, which has quite a list of "aliases," is a common parasite of dogs and cats in Japan, Korea and China, and also in Palestine and the Balkans. Human infection is very common and widespread in Japan. Like other members of the family, this tiny fluke is not very particular about its final host, for it not only infects carnivores, pigs and man, but also pelicans, and, experimentally, mice.

The adult worms live in the duodenum, sometimes by thousands. They are only 1 to 2.5 mm. in length and about 0.5 mm. broad. A characteristic feature is the displacement of the ventral sucker to the right side of the body, with the genital opening in a pit at the anterior border of it. The eggs are small, oval, and brown, about 28 to 30 μ by 16 to 17 μ, without the mosaic markings of the shell which characterize eggs of the Opisthorchidæ. The life cycle was first studied by Muto (1917). The eggs contain developed miracidia when laid. The snails which serve as intermediate hosts are species of *Melania*, as in the case of *Paragonimus*. *M. libertina* and *M. ebenina* have so far been incriminated. The parthenitic generations consist of sporocysts and two generations of rediæ. The cercariæ behave like those of *Clonorchis*, and attack fresh-water fishes, particularly a species of trout, *Plectoglossus altivelis*, and infection of the final host occurs when the uncooked fish are eaten.

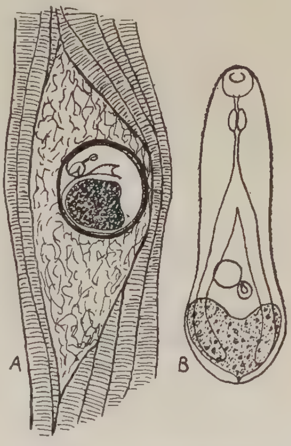

FIG. 97. Metacercariæ of Heterophyes. *A*, cyst in muscles of mullet; *B*, metacercaria freed from cyst. × 50. (After Witenberg.)

Heterophyes heterophyes (Fig. 96) is also a very small fluke; relaxed specimens in dogs measure up to 2.7 mm. by 0.9 mm., but in cats they are only about 1.3 by 0.3 mm. They have the ventral sucker on the median line, with a separate genital sucker to the right of it. This fluke lives in cats, dogs and allied animals in Egypt, Palestine and the Far East. According to Witenberg (1929) they are the commonest parasites of these animals in Jerusalem. The life cycle has not been completely worked out, and the snail host is unknown, unless certain cercariæ found in *Melanoides tuberculatus* and *Cleopatra bulimnoides* in Egypt are proved to belong to this species, as is believed. The cercariæ are known to encyst under the scales and in the flesh of mullets, especially *Mugil cephalus*, and rarely in other fish; in one case Witenberg found over 1000 cysts per gram of flesh in a mullet from the fish market in Jerusalem. The round cysts (Fig. 97) lie in spindle-shaped masses of fat globules and measure from 0.13 to 0.26 mm. in diameter. The metacercariæ, lying folded inside, have the anterior part of the body flattened and the posterior part rounded and distended by a large excretory vesicle. It is a common human parasite in Egypt, and the eggs are often found in human feces in Palestine, and *H. nocens* and *H. katsuradai,* found in man in Japan, are either the same or very closely related species. Various other Heterophyidæ, found in night herons, can also infect cats and dogs, and have been found to parasitize man experimentally, and probably do so occasionally in nature. They all use species of *Melania* (Fig. 81) as first intermediate hosts, and subsequently encyst in small fresh-water fishes.

The tiny Heterophyid flukes deeply invade the mucous membranes, where they become attached by their suckers, but they cause very little injury, and the symptoms are usually negligible, though in heavy infections there may be mild digestive disturbances and diarrhea. Faust and Nishigori (1926), in the course of experimental infections of mammals with some species found in night herons, observed that as these flukes grow older they gradually shift their positions farther and farther back in the gut, until conditions are finally unsuitable for them, and they are then spontaneously expelled. Faust (1929) considers this a normal phenomenon, and thinks that the body is thus gradually freed from the parasites, but it seems likely that the backward movement is correlated with the development of the worms in an abnormal host, and might not occur in the normal host.

Like other intestinal flukes, these species are susceptible to the nematode group of anthelmintics (see p. 249), but on account of their small size and ability to hide away between the villi, it is not likely that the results of treatment will prove very satisfactory unless the intestine is thoroughly cleaned of débris and mucus by means of salts beforehand. Prevention consists in eschewing raw infected fish.

Echinostomes. — The family Echinostomatidæ includes a large number of flukes, most of which are parasitic in cold-blooded vertebrates and birds, and comparatively few in mammals. They are strikingly variable in their life cycles, and may not, as Faust suggests, constitute a natural group. The life cycles of only a few are known, but of some of these the cercariæ encyst in their mother rediæ, of others in the snail host, of others on water vegetation, and of others in the flesh of insects or fishes. The eggs are large, usually over 100 μ in length, and contain partly developed embryos when laid; the miracidia have a median eye spot and develop in water; in the snail host they are thought to transform directly into rediæ instead of sporocysts. The adults are at once recognizable by the presence of a collar of large spines near the anterior end; this is also present in the cercaria, and is structurally like that of the adults of the various species. All kinds of water birds are very commonly infected with these flukes.

A number of species of echinostomes have been recorded from man, most of them only in one or a very few cases. These include *Echinostoma ilocanum* (Fig. 98*C*), in some native prisoners in Manila; *E. malayanum* (Fig. 98*B*), in two cases in Malaya; *E. sufrartyfex*, in one case in Assam; *E. jasseyense*, (Fig. 98*A*) in one case in Roumania; *E. macrorchis*, in one case in Japan; and *Echinochasmus perfoliatus* (Fig. 98*D*), in a few cases in Japan. Of the first four species nothing is known beyond their rare occurrence in human beings; *E. macrorchis* is a rat parasite in the Far East, and *Echinochasmus perfoliatus* is a parasite of cats and dogs in Central Europe, India and the Far East. This species has been proved to reach its final host by encysting in various species of fresh-water fish, but nothing is known of the life cycles of the others. They are merely medical curiosities. The eggs, when found, can be distinguished from other large fluke eggs, such as those of amphistomes and Fasciolidæ, by the partly developed embryos contained in them.

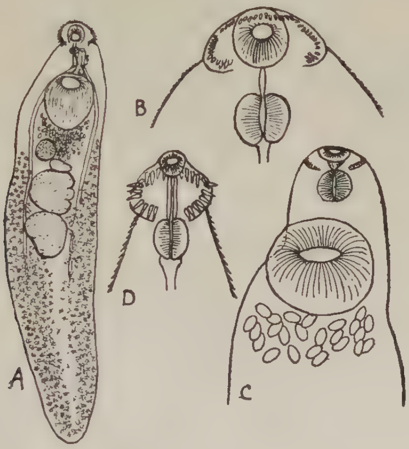

Fig. 98. Echinostomes of man. *A*, *Echinostoma jasseyense*, showing arrangement of organs (two testes and seminal receptacle behind the ovary, uterus between sex glands and ventral sucker); *B*, head of *E. malayanum; C*, head of *E. ilocanum; D*, head of *Echinochasmus perfoliatus*. *A*, × 10, after Léon and Ciurea; *B* and *C*, × 30, after Leiper; *D*, × 30, after Tanabe.

CHAPTER XIII

THE TAPEWORMS

General Structure.—Even more peculiar and remarkable in their structure and life than the flukes are the tapeworms. A mature tapeworm is not an individual, but a whole family, consisting sometimes of many hundreds of individuals one behind the other like the links of a chain (Fig. 99). In some respects the tapeworms are more degenerate than flukes, due to their invariably parasitic life in the digestive tract of their hosts. Being continually bathed in semi-digested fluids in the intestine they can readily absorb food all over the surface of their bodies, and have no need for a digestive system of their own. The digestive tract, therefore, is entirely lacking, not even a vestige of it remaining as an heirloom from less dependent ancestors, even in the larval stages.

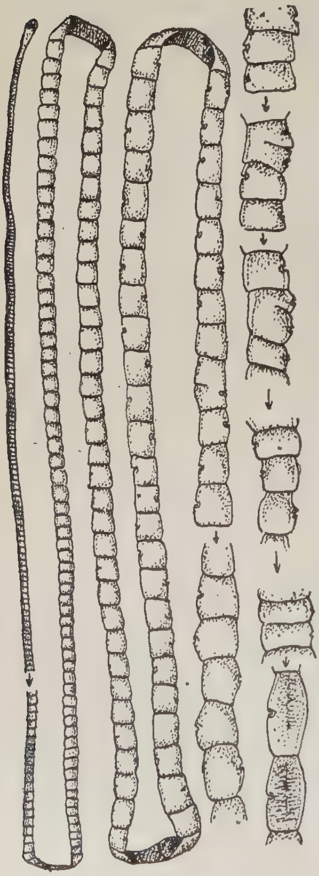
FIG. 99. Beef tapeworm, *Tænia saginata*, × $\frac{2}{3}$. Note small head, gradual change in size of proglottids, and irregular alternation of sides of genital apertures. (After Stiles.)

In general form the majority of tapeworms are very long tapelike organisms which attach themselves to their host's intestinal walls by a "head" or scolex, though some zoölogists consider this to be in reality the posterior end of the worm. Next to the head there is a narrow region or "neck" which continually grows and, as it does so, forms constrictions, thus constantly budding off new segments. The segments, however, remain connected internally by the musculature and also by nerve trunks and excretory tubes. As the newly formed segments push ahead the segments previously formed, there is produced the characteristic chain of segments, each of which is known as a proglottid. The proglottids just behind the neck are, of course, the youngest; they are at first indistinct, and have no differentiation of internal organs. As they are pushed farther and farther from the scolex, the organs progressively develop, so that it is possible, in a single tapeworm, to find a complete developmental series of proglottids from infancy to old age; the young undifferentiated segments just behind the neck gradually attain sexual maturity in the middle portions of the worm, and then there follows a gradual decadence of these organs as the segments " go to seed " and become filled full by the pregnant uterus with its hordes of eggs. The whole process can be likened to the development of an undifferentiated bud into a perfect flower and then a seed pod.

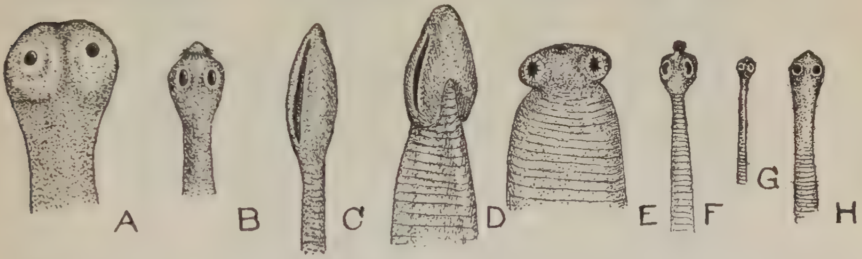

FIG. 100. **Heads of some adult tapeworms found in man, drawn to scale;** *A*, **beef** tapeworm, *Tœnia saginata; B*, pork tapeworm, *T. solium; C*, fish tapeworm, *Diphyllobothrium latum; D*, heart-headed tapeworm, *Diphyllobothrium cordatum; E*, African tapeworm, *T. africana; F*, double-pored dog tapeworm, *Dipylidium caninum; G*, dwarf tapeworm, *Hymenolepis nana; H*, rat tapeworm, *Hymenolepis diminuta.* × 10.

The scolex of a tapeworm serves primarily as an organ of attachment, though it also contains what little brain a tapeworm has. Considering the entire class Cestoda, the variety of holdfast organs which are developed by the scolex is remarkable, consisting of groove-like, in-cupped or ear-like suckers, and in addition, in some species, crowns of powerful hooks or rows of spines, and in one group long protrusible spiny proboscides; the scoleces of the tapeworms infesting mammals, however, are comparatively monotonous in form (Fig. 100).

The nervous system consists of a few ganglia and commissures in the scolex from which longitudinal nerve cords run through the length of the worm, the largest ones being a pair at the lateral borders. Coördination of movement is very limited, though the whole worm can contract at once, as for example when dropped into cold water. Individual ripe segments, when detached, show considerable sensitiveness and often astonishing motility. The excretory system is fundamentally of the same type as in flukes, and consists typically of two pairs of lateral longitudinal tubes, one larger than the other, connected by a prominent transverse tube near the posterior end of each proglottid, and sometimes by a network of smaller tubes. From the main canals fine tubules ramify in the packing tissue or "parenchyma" of the worm and end in flame cells. The first-formed proglottid has a terminal bladder as in flukes, but this is lost when this proglottid is cast off, and subsequently the excretory tubes open separately at the end of the last segment still attached. The muscular system consists of longitudinal, transverse and circular fibers, much better developed in some species, which are thick and fleshy, than in others which are thin and semi-transparent.

As of flukes, the main business of tapeworms is the production of myriads of eggs in order to safeguard the species against extermination in the perilous transfer from host to host. Each proglottid possesses complete reproductive systems of both sexes, fully as complete as in the flukes, if not more so (Fig. 101), and in some species there is even a doubling of both sets of organs in each proglottid. The female system consists of an ovary, which may be single or in two more or less distinct lobes; yolk glands, either in a single or bilobed mass, or scattered through the segment; a cluster of shell glands around an oötype, where the component parts of the egg are assembled; a vagina for the entrance of the sperms, with an enlarged chamber, the seminal receptacle, for storage of sperms; and a uterus, which may or may not have an exit pore. In the tapeworms which have a pore (Pseudophyllidea) the development and extrusion of eggs goes on continuously in many segments at once, but in the higher tapeworms, after a temporary period of egg production, the necessity for storage of the eggs causes the uterus to develop enormously by the formation of branches or sacs, so that it

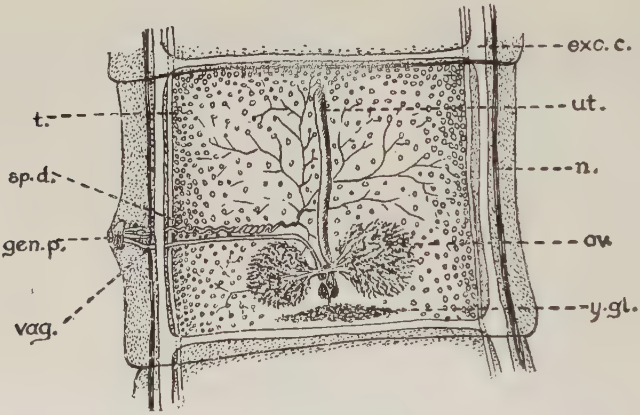

FIG. 101. Sexually mature proglottid of beef tapeworm, *Tænia saginata; exc. c.*, excretory canal; *n.*, nerve cord; *ut.*, uterus; *ov.*, ovary; *y. gl.*, yolk gland; *vag.*, vagina; *gen. p.*, genital pore; *sp. d.*, sperm duct; *t.*, testis. × 7. (Partly after Leuckart.)

eventually comes to occupy practically all of the segment between the lateral excretory and nerve trunks, and the other organs atrophy. The form of the " ripe " uterus varies in different genera and species, and is often useful in identification (Fig. 102). The male system consists of a variable number of scattered testes, connected by minute tubes with the sperm duct or vas deferens, which is usually convoluted, and may have an enlargement for storage of sperms, the seminal vesicle. The end of the vas deferens is modified into a muscular intromittent organ, the cirrus, which is retractile into a cirrus pouch or sac. In most tapeworms both cirrus and vagina open into a common cup-shaped

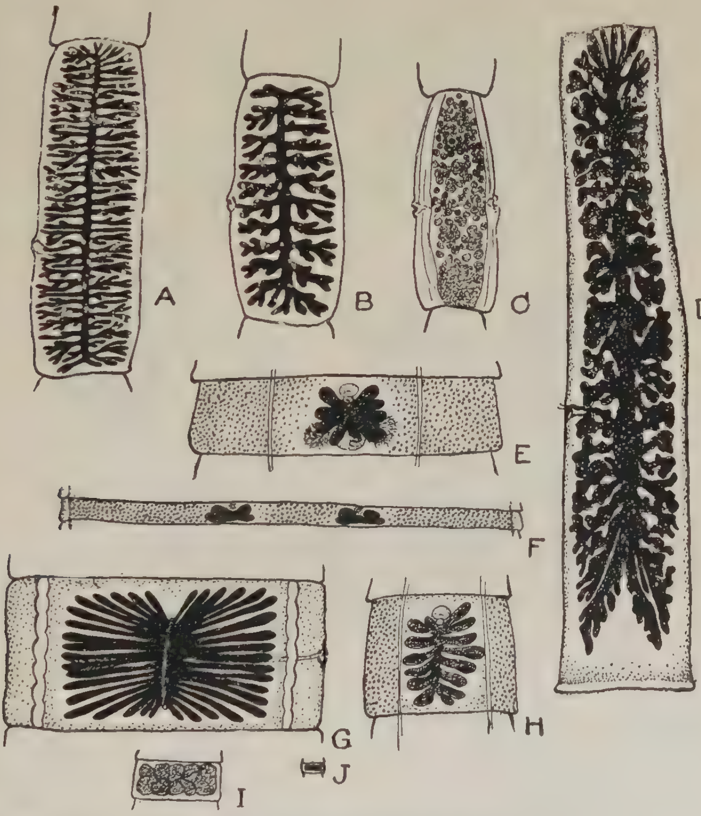

Fig. 102. Ripe proglottids of various tapeworms of man, drawn to scale according to average measurements: *A*, *Tænia saginata* (after Leuckart). *B*, *Tænia solium* (after Stiles). *C*, *Dipylidium caninum* (after Diamare). *D*, *Tænia confusa* (after Guyer). *E*, *Diphyllobothrium latum* (after Leuckart). *F*, *Diplogonoporus grandis* (after Ijima and Kurimoto). *G*, *Tænia africana* (after von Linstow). *H*, *Diphyllobothrium cordatum* (after Leuckart). *I*, *Hymenolepis diminuta* (after Grassi). *J*, *Hymenolepis nana* (after Leuckart).

chamber or atrium, with a pore on either the lateral border or the midventral surface. Either self-fertilization of a single segment, or cross-fertilization between different segments of the same or other worms, can occur, but probably self-fertilization is commonest. As a rule the male reproductive organs mature before the female.

The life cycle is not quite so complicated as in flukes and does not involve parthenitic generations, although in some species the larval forms multiply by budding. In a great many tapeworms, especially of fishes, the life cycle is unknown; in fact, it was not until the middle of the last century that Küchenmeister proved that the bladderworms in pigs and cattle were in reality the larvæ of the common large tapeworms of man; previous to that time they were classified in a separate order, "Cystica."

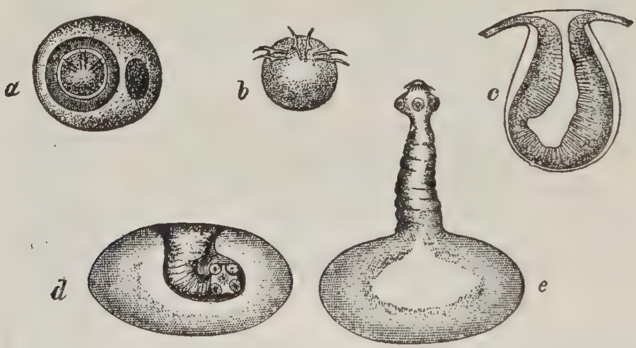

Fig. 103. Stages in life cycle of *Tænia solium*. *a*, egg containing embryophore; *b*, hatched oncosphere; *c*, invagination in cyst wall, at the bottom of which the scolex will form; *d*, cysticercus with head invaginated; *e*, same with head evaginated. (After Blanchard from Brumpt.)

The eggs of tapeworms develop within themselves little spherical embryos characterized by the presence of three pairs of claw-like hooks, whence they are known as oncospheres (Fig. 103 *A* and *B*). One or two enclosing membranes, inside the egg shell proper, form about the developing embryo, the inner of which is called the embryophore. In the order Pseudophyllidea this has a ciliated epithelium and the embryos, called coracidia (Fig. 106*B*), have a brief free-swimming existence, like miracidia, in which they roll about by means of their cilia long enough to attract the attention of copepods which devour them, and which serve as first intermediate hosts. In these they change into elongated oval "procercoids" (Fig. 106*C*), comparable with sporocysts, but solid, and incapable of parthenogenetic reproduction. The six hooks are still present on a small caudal appendage. Further development into a "plerocercoid" (Fig. 104*C*) occurs only when the infected copepod is eaten by a fish or other animal. The plerocercoids are solid worm-like larvæ with a scolex invaginated at one end; when the animal containing them is eaten by the final host the scolex turns right side out and attaches itself to the intestinal wall, and the mature tapeworm develops.

In the order Cyclophyllidea, on the other hand, the oncosphere remains in the egg surrounded by the non-ciliated embryophore, entirely passive, until eaten by the intermediate host. Here it transforms into a bladder-like structure, a part of the wall of which differentiates into one or more scoleces turned inside out (invaginated) (Fig. 103 *C* and *D*). In some cases the whole embryo becomes hollow and grows into a large bladder, into the spacious cavity of which the relatively small scolex or scoleces are invaginated; such a larva is called a *cysticercus* if there is only one scolex, and a *cœnurus* (Fig. 111) if there are a number of them; in one tapeworm, *Echinococcus*, the bladders add a further method of multiplication by budding off daughter and grand-daughter bladders, and the bladder walls, instead of directly producing scoleces, first produce brood-capsules, each of which in turn produces on its walls a number of scoleces, whereby one huge larval cyst, called a *hydatid*, may be the mother of many thousands of tapeworms (Fig. 113). In other cases the main portion of the body of the embryo remains solid and grows very little, while one end of it becomes hollowed out into a small bladder which is practically filled by the invaginated scolex (Fig. 104*B*). The undeveloped solid portion remains as a " caudal appendage." Such a larva is called a *cysticercoid*, and is characteristic of those tapeworms which use insects as intermediate hosts. On being eaten by a final host only the scoleces survive; these turn right side out (evaginate), attach themselves to the mucous membrane of the intestine, and grow each into a mature tapeworm. In one progressive genus, *Hymenolepis*,

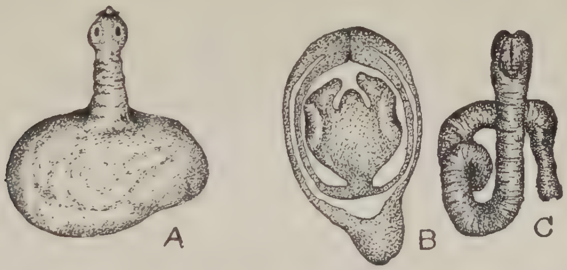

FIG. 104. Types of tapeworm larvæ: *A*, cysticercus of *Tænia solium* with head and neck evaginated, × 3; *B*, cysticercoid of *Hymenolepis nana*, × 120; *C*, plerocercoid of *Diphyllobothrium latum*, with head invaginated. (*A*, partly after Stiles, *B*, from several figures by Grassi and Rovelli; *C*, partly after Braun.)

a few species have broken away from the traditional intermediate host idea, and complete their development in one host; the cysticercoids develop inside the intestinal villi, and subsequently gain the lumen of the intestine where the mature phase is attained. For a long time parasitologists were very skeptical of the truth of such unorthodoxy on Nature's part.

Classification. — The classification of the Cestoda is much more satisfactorily worked out than that of the Trematoda. There are usually recognized two subclasses, Cestodaria, in which the body is unsegmented and fluke-like, without a scolex, and containing a single set of reproductive organs, and the true Cestoda, in which the body is more or less clearly segmented with the reproductive organs repeated in each segment, and in which there is a definite scolex. The Cestodaria are fish parasites; only the true Cestoda concern us here. Of these, four orders are usually recognized, though Southwell (1925) added a fifth one for a few aberrant forms which do not fit into the other four. The classification, based mainly on the structure of the scolex, is as follows:

Order 1. *Pseudophyllidea.* Head with two lateral, or rarely one terminal, sucking grooves called " bothria "; proglottids nearly all in same stage of development; vitelline glands scattered in the segments.

Order 2. *Cyclophyllidea.* Head with four in-cupped suckers; proglottids in all stages of development; vitelline glands compact and unpaired, near ovary.

Order 3. *Tetraphyllidea.* Head with four suckers in the form of earlike or lappet-like outgrowths; proglottids in various stages of development; vitelline glands scattered, in two lateral rows or in broad dorsal and ventral layers.

Order 4. *Trypanorhyncha.* Head with two or four bothria and four long evertible proboscides armed with spines, retractile into sheaths, otherwise like Tetraphyllidea. Adults only in spiral valve of sharks and rays.

Order 5. *Heterophyllidea.* A few aberrant tapeworms of fish, with heads unlike any of those above.

It is only the first two of these orders which contain species which attack man. Although 25 different species of tapeworms have been recorded as attacking man, 7 as larvæ and 19 as adults, there are only 4 adult species and 3 larval species which are at all common. The order Pseudophyllidea contains one in each group, *Diphyllobothrium latum* as an adult, and *D. mansoni* as a larva; the order Cyclophyllidea includes as adults *Tænia solium*, *T. saginata*, and *Hymenolepis nana*, and as larvæ *Tænia solium* and *Echinococcus granulosus*. *Hymenolepis diminuta* and *Dipylidium caninum* are other species of which 50 to 100 or more cases are on record, and which are probably much less rare than the records indicate, but all of the others, some of which are briefly mentioned in the following pages, are rare indeed.

Diagnosis. — Fluke and nematode parasites of the digestive system are usually diagnosed by finding the eggs of the worms in the feces by microscopical examination, but this method is not of universal application in the case of tapeworms. The Pseudophyllidean tapeworms (*Diphyllobothrium* and related worms) can be diagnosed in this way, since the operculated eggs are expelled through the uterine pores of many proglottids at a time, and are therefore always present in the feces. Like the eggs of flukes, these eggs do not float in saturated salt solution, and can be concentrated only by straining and sedimenting or centrifuging in water. *Hymenolepis* infections can also be diagnosed by fecal examination for eggs, even though no birth pore is present, since the segments broken off from the ends of the worms commonly disintegrate and rupture before leaving the body of the host. *Hymenolepis* eggs are easily found by floatation methods. *Tænia* infections, on the other hand, as well as many of the rarer infections of man and many other common tapeworm infections of animals, cannot be reliably diagnosed in this manner, since the segments commonly escape from the body, uninjured and still alive. In this case search must be made for the voided segments in the stools; the shape of the segment and form of the gravid uterus serves to identify the species. In worms like *Tænia* and *Dipylidium*, which have elongated segments, the latter are found singly or in short chains of two or three, but in some of the tapeworms with broad and very short proglottids, like those of the family Anoplocephalidæ, which includes many common tapeworms of herbivorous animals and one rare parasite of man, the segments are often shed in blocks of more numerous segments. *Tænia* eggs, or rather embryophores escaped from the eggs, are present in the feces whenever segments rupture, which appears to be a fairly frequent occurrence; the thick, brown, striated embryophores are porous, and therefore cannot be found by floatation.

The eggs of *Diphyllobothrium* may be confused with those of flukes, but the shell is thinner and more transparent, and the operculum, in fresh eggs, is very inconspicuous. They are different in size from any common human fluke eggs, but come nearest to those of *Paragonimus*, which, however, average larger. Other tapeworm eggs of man are all recognizable as such by their six-hooked embryos. There is no possibility of the confusion of *Tænia* and *Hymenolepis* eggs when one has once seen them, but many inexperienced physicians, unfamiliar with *Hymenolepis*, take all eggs with six-hooked embryos to be *Tænia*, sometimes with disconcerting results. A physician once complained to the writer that he was unable to expel even a few segments of a tapeworm by the use of male fern; it developed that he was hunting for expelled tæniæ when he had found only *Hymenolepis* eggs. In another case a physician found tapeworm eggs in the stool of a high-class Indian Brahmin, and mortally offended him by telling him he had eaten insufficiently cooked beef or pork, when in reality the eggs were those of *Hymenolepis.*

Pathogenicity. — The damage done by adult tapeworms to their hosts is often either under- or overrated. There are some who believe that the presence of a tapeworm is more or less of a joke, and as such to be gotten out of the system but not to be taken seriously, while there are others who become unnecessarily disturbed over them. They may cause mechanical injury by obstructing the intestinal canal, and by injuring the mucous membranes where they adhere, and they may absorb enough nourishment to produce the proverbially ravenous " tapeworm appetite." They undoubtedly do some injury by producing toxic substances that are absorbed, and which cause such symptoms as anemia, eosinophilia, malaise, and indefinite nervous symptoms, such as dizziness, insomnia, restlessness, false sensations, and occasionally convulsions and epileptic fits. Disordered appetite, abdominal discomfort, anal itching, etc., may also be complained of. The writer knows of a patient who came to a physician for treatment thinking he had tuberculosis, and having been so diagnosed by another doctor. He was in anemic condition, weak and easily exhausted, and subject to mental disturbances. His cheeks were sunken, his frame emaciated, and his eyes staring. Within a fortnight after two large tæniæ had been expelled he was like a new man, though he had been suffering for over a year. On the other hand, I had a colleague who had harbored a *Tænia* for years; in spite of a number of unsuccessful efforts to part company with it, " Horace," as he familiarly called his guest, stayed with him, yet there were never any symptoms other than segments in the stools, and the host continued in ruddy and robust health. The latter case is, I believe, much more common than the former.

Not all the tapeworms are equal in their pathogenicity. The " broad tapeworm," *Diphyllobothrium latum*, sometimes appears to cause a severe type of anemia, in which the corpuscles are reduced to 2,000,000 per c.mm. or less, and the hemoglobin to 25 or 30%. Worthin (1928), describing cases in northern United States, says that they all present more or less severe anemia, in some instances suggesting strongly a pernicious anemia. He examined at autopsy one very severe form of hemolytic anemia in which two *D. latum* were present. After expulsion of the worms all symptoms of anemia disappear. Recently the interesting observation has been made that eating a half-pound of liver daily, or partaking of a diet rich in liver extract and vitamines, removes the anemia and other symptoms, even without expulsion of the worm. *Hymenolepis nana* very commonly causes rather severe toxic symptoms, especially in children, including abdominal pain, diarrhea, convulsions, epilepsy, insomnia, and the like. The tæniæ are somewhat less prone to produce such symptoms, especially in adults.

Treatment. — Since the generative part of a tapeworm is the neck region immediately behind the head, it is necessary that the head be expelled, for if the worm breaks off behind the head, as very commonly happens in unsuccessful treatments, a whole new worm is generated in a few weeks. Since the head is usually buried deep down between the intestinal villi, and since the weight of a drug-stupefied worm dragging on the head in response to the intestinal movements stimulated by a purgative are very likely to cause it to break, it is necessary, in order that the chances of success be at all promising, that the intestine be thoroughly prepared before the drug is administered. The patient has to be starved or at least kept on a broth diet for not less than 36 hours, and must then be given a large dose of salts on the evening preceding treatment.

The drugs which have been found most useful in expelling tapeworms constitute a group distinct from those which act most efficiently against nematodes. They include (1) a group of vegetable extracts from *Filix mas* or male fern, cusso, and kamala, all of which are derivatives of a substance known as phloroglucin; (2) pelletierine, an alkaloid derived from pomegranate bark; (3) arecoline and allied alkaloids from areca nuts; and a few other remedies, such as ground pumpkin seeds. The classical nematode anthelmintics, such as thymol, chenopodium and carbon tetrachloride, are of little avail, although Tomb (1923) has reported successful results with small doses of beta-naphthol repeated every morning for a week.

After the drug is given another purge should follow, to wash the worm out of the intestine. It should be passed into a vessel of warm water since sudden contact with cold water may cause a sudden contraction which is sufficient to break the worm before the head has released its hold. The parts of the worm should always be kept and examined to find out whether more than one are present, and a search should be made for the indicated number of heads. If one attempt to expel the heads is not successful, the treatment should not be repeated until after several weeks, to allow time for the worms to grow out again. The chances of dragging away the head are then better.

In the case of *Hymenolepis nana*, since this worm is so small and so like a strand of mucus as to be seldom found in the feces, and since it usually occurs in large numbers, this method of determining the success of a treatment cannot be used. The segments of this worm, however, usually disintegrate and liberate the eggs before leaving the body, so the success of treatment can be determined by a search for the eggs (see p. 210).

Prevention. — Prevention varies, of course, with the species of tapeworm and its intermediate host, but since infection with all the common human species, with the exception of the species of *Hymenolepis*, results from eating raw or imperfectly cooked beef, pork or fish in which the bladderworms have developed, the exclusive use of thoroughly cooked meat and fish is the best preventive measure. Experiments show that pork bladderworms are killed when heated to 127° F. and beef bladderworms to 120° or even less, but the difficulty of heating the center of a large piece of meat even to this point is shown by the fact that in an experiment to test the penetration of heat, a ham cooked by boiling for two hours had reached a temperature of only 115° in the center. When roasted, pork should always be cut into pieces weighing no more than three or four pounds to insure thorough penetration of heat. Beef which has lost its red or " rare " color is quite safe.

Since bladderworms are unable to survive the death of their host for more than a limited time, they are eventually destroyed by ordinary cold storage — within three weeks in the case of the beef bladderworm, *Cysticercus bovis*, but not always so soon in the case of the pork bladderworm, *C. cellulosæ*. According to Dr. Ransom temperatures of about 15° F. kill beef bladderworms within five days. Thorough curing or salting of meat is also destructive to the parasites.

The meat of sheep, goats or chickens do not convey any parasites to man.

Infected persons should be careful not to contaminate the food or water of domestic animals with their feces, bearing in mind the various ways in which the eggs may be disseminated — by streams, rain, flies, etc.

The eggs of the dwarf tapeworm, *Hymenolepis nana*, develop through the bladderworm stage to the adult in a single host, and must therefore be guarded against by different measures (see p. 283). The larvæ of other species of *Hymenolepis* develop in insect larvæ such as meal worms, and are therefore subject to still different means of prevention.

Order Pseudophyllidea

All the members of the Pseudophyllidea which live in man or domestic mammals are members of the family Diphyllobothriidæ. These are large worms consisting of long chains of numerous segments, and with a slender head provided with a slit-like groove or bothrium on either side. The majority of the segments are mature and functional at one time, and deposit eggs through the uterine pores as more are being developed. Eventually, as old age overtakes them, the proglottids cease to produce more eggs, they gradually empty their uteri, and then, shrunken and twisted, are finally sloughed off in long chains. The general type of life cycle has already been described.

One Pseudophyllidean tapeworm, *Diphyllobothrium latum*, is a common human parasite in its adult stage, while another species of the same genus, *D. mansoni*, commonly infests man in its larval stage.

Diphyllobothrium latum. — This worm, sometimes called the "broad" tapeworm and sometimes the "fish" tapeworm, because infection is derived from eating fish, is the largest and also the most injurious tapeworm to which human beings are subject. In earlier literature it is referred to as " Dibothriocephalus," but this name properly belongs to a different group of tapeworms which reach the adult stage in fishes. *D. latum* has been known for centuries as a common human parasite in many parts of Central Europe and in the Baltic countries, and more recently has been found widely distributed also in eastern Europe, central Asia, Manchuria and Japan, as well as in Madagascar and a few places in Africa and in North America. In recent times the Baltic immigrants around the Great Lakes and Canada have established the parasite in Minnesota, northern Michigan and around lakes in the Canadian forests, and it is becoming annually more common among native Americans. Man is an important host, but the worm also develops in dogs, cats and other fish-eating mammals. In the forested areas of Canada Vergeer (1929) has shown that the worm, undoubtedly originally brought in with the Finns and Scandinavians who were almost exclusively employed in early lumbering operations, became established in fish of the Canadian lakes and has since then not only kept alive but has been widely distributed in small lakes by dogs, which are fed almost entirely on raw fish by the Indians and white settlers of the Canadian woods. Wild Carnivora, especially bears, which Vergeer has found susceptible, undoubtedly help in the perpetuation of the parasite, for bears are fond of fish and commonly scoop them out of small streams in the spawning season.

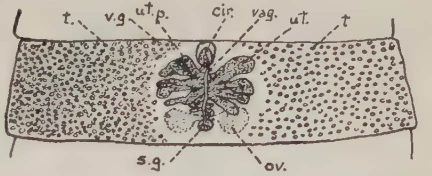

FIG. 105. Mature segment of *Diphyllobothrium latum*. *cir*, cirrus sac; *ov.*, ovary; *s.g.*, shell gland; *t*, testis; *ut.*, uterus; *ut. p.*, uterine pore; *vag.*, vagina; *v.g.*, vitelline glands; testes shown on both sides, vitelline glands only on left. × 6. Original.

D. latum is a veritable monster, reaching a length of from 10 to over 30 feet, with a width of from 10 to 12 or even up to 20 mm., and with a total of 3000 to 4000 proglottids in large specimens. The slender scolex is almond-shaped (Fig. 100*C*). The proglottids for the most part are much broader than long, although the terminal ones become approximately square. The arrangement of the organs is shown in Fig. 105. The rosette-like coiling of the uterus distinguishes this species from most others of the genus, except *D. cordatum*.

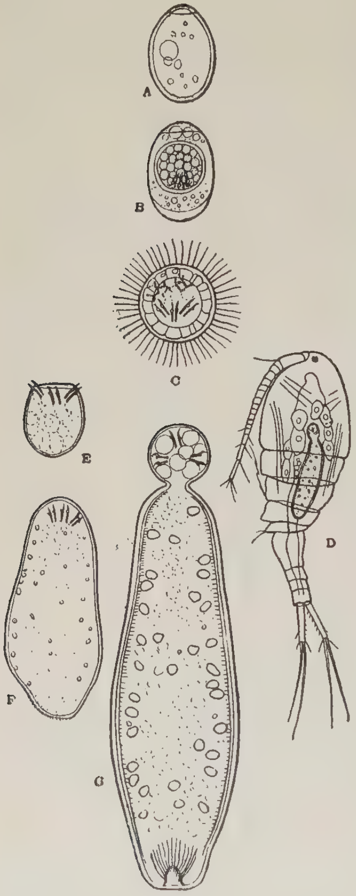

FIG. 106. Developmental stages of *Diphyllobothrium latum*. *A*, undeveloped egg; *B*, egg containing developed embryo; *C*, free embryo or coracidium; *D*, *Cyclops strenuus* containing procercoid; *E*, embryo after shedding ciliated envelope in *Cyclops; F*, growing procercoid; *G*, full-grown procercoid. (After Brumpt.)

The broadly oval, operculated eggs, which average about 70 by 45 μ, contain abundant yolk cells (Fig. 106*A*). The eggs require from eight or ten days to several weeks for the ciliated embryos to mature, depending on temperature. The embryos, or coracidia (Fig. 106*C*), 40 to 55 μ in length, hatch and swim about by means of their cilia, though they often slip out of their ciliated envelopes and creep on the bottom. The embryos were shown by Janicki and Rosen (1917), and Essex (1927) to develop in certain species of copepod crustaceans, *Cyclops* and *Diaptomus*, into larvæ called procercoids (Fig. 106 *D* and *G*).

In Europe *Cyclops strenuus* and *Diaptomus castor* were found to serve as hosts for the procercoids, and in the Great Lakes region of the United States *C. brevispinosus*, *C. prasinus* and *D. oregonensis*; many related species failed to function as hosts. Li and Faust observed that some species of Cyclops feed on the coracidia much more readily than do others.

Soon after the coracidia are ingested by the copepods they lose their ciliated covering, and a naked oncosphere, only 24 μ in diameter, is liberated in the intestine and bores through into the body cavity.

In 12 to 15 days it is a solid, sausage-shaped creature, 0.4 mm. long, with an oval or spherical appendage carrying the embryonic hooks. This appendage shrinks and a cup-shaped depression appears at the opposite end; a large portion of the body is occupied by a central pyriform mass. The full development is reached in two or three weeks, when the larvæ are about 0.5 mm. long. Further development occurs in fish when the infected copepod is eaten. The passage through the intestine and body cavity of the fish is slow; it requires about six days for the larvæ to reach the liver in young fish, and in older fish it may take two or three weeks. Finally the larvæ reach the flesh of the fish and grow into elongated worm-like plerocercoid or "sparganum" larvæ, from 4 or 5 mm. to several centimeters in length. They are not encysted and are found anywhere in the flesh and sometimes in fatty tissue among the viscera, in the gonads, or in the intestinal walls; the smaller ones lie straight, but with growth they become increasingly bent and twisted (Fig. 107). The anterior end has a depression which is the withdrawn and inverted scolex, while the remainder of the body is white, somewhat flattened, and marked by irregular wrinkles, but without segmentation. In uncooked fish their opaque white color shows clearly through even 0.5 cm. of translucent flesh, but they may be confused with cysts of flukes or other tapeworms if not carefully examined. Cysts of tapeworms of the genus *Proteocephalus* are often present, but these have four or five cup-shaped suckers on the head; some of the other plerocercoids found in herring, perch, trout, etc. are more difficult to distinguish. The fish involved as second intermediate hosts are mostly carnivorous species, such as trout, burbot, perch, and pike; in America various species of pike and pickerel (*Stizostedeon* and *Esox*) are the most important hosts, and there is no evidence that perch or trout become infected in this country. These large carnivorous fish do not feed intentionally on

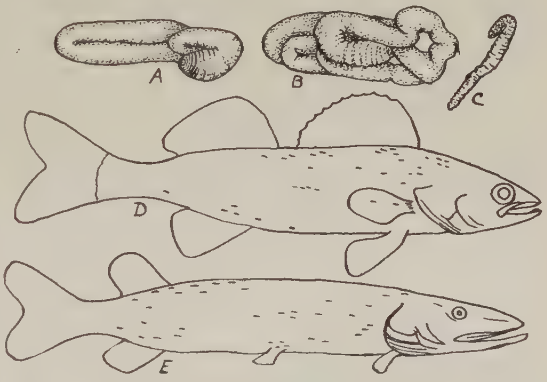

Fig. 107. *A* to *C*, plerocercoid larvæ of *D. latum* as they appear in the flesh of fishes, × 3; *D*, outline of a wall-eyed pike (*Stizostedeon*) showing distribution of 35 plerocercoids in the flesh; *E*, same of pickerel (*Esox*) with 37 plerocercoids. (After Vergeer.)

copepods, and probably ingest them in the stomachs of smaller fish on which they prey. Infection of the final host usually results from eating imperfectly cooked flesh or roe of infected fish, or from conveying small plerocercoids to the mouth by the hands, to which they cling while fish is being cleaned. In three weeks they may have reached a length of three feet, and may begin producing eggs in that time. Nicholson (1928) estimates that one worm produces 36,000 eggs daily.

The epidemiological conditions as they exist in northern United States are about as follows: Finns and other Baltic peoples have settled in large numbers about the lakes, many having brought worms with them "from the old country." The lake towns pour their sewage directly into the lakes, and the inhabitants fish for the prized pike, which commonly harbor the plerocercoids, near the sewage outlets. The Finns serve raw fish with sour milk, and fishermen eat it with a sprinkling of salt after removing the skin. Summer visitors in camps and hotels often partake of fish hastily prepared, content with a well-done exterior. Such people may develop infection and start new endemic foci in other places. Dogs and cats are usually given the raw refuse, and help to keep the infection alive. Furthermore, millions of pounds of wall-eyed pike and pickerel are annually imported from infected Canadian lakes, nearly all shipped fresh to meet the demands of Jewish trade; Vergeer (1929) found 256 plerocercoids of *D. latum* in 214 such fish which he examined, and estimates that on this basis the United States annually imports over 5½ million plerocercoids of this dangerous tapeworm. In some small lakes 50 to 75% of the pikes and pickerels were found infected.

Control of *D. latum* infection must depend mainly on more careful abstinence from fish not thoroughly cooked. Vergeer, in discussing this question, thinks it would be well if many persons were to cook fish twice as long as they are accustomed to. However, although worms cooked in the flesh cannot produce infection, the eating of cooked worms is not esthetic. The danger could be reduced in the United States by 80% by the exclusion of Canadian fish, but such a measure would cause great economic loss to Canadian fishermen and others who participate in the business. By adequate publicity the public could be prevented from eating half-cooked fish, housewives and cooks from tasting raw fish to test their skill in flavoring, and children from being allowed in kitchens when the fish is being prepared. Posters informing the public of infected waters; regulations concerning the pouring of raw sewage into lakes or streams, or pollution of waters by individuals; efforts to find and treat as many cases as possible; examination and treatment of immigrants from infected countries; and efforts to reduce infection in dogs and cats by propaganda against feeding them raw fish; these are measures which have been suggested for the control of *D. latum* infections. Since, however, wild carnivores also serve as reservoir hosts, and extermination of these animals to prevent infestation of fish with tapeworm larvæ is unthinkable, complete eradication of fish infestation is beyond human control, and it is therefore necessary to devise adequate means of killing the larvæ before fish is eaten, and preferably before it reaches the consumer.

There are a few records of human infection with related worms. *Diphyllobothrium cordatum* is a rare human parasite, normally found in seals, walruses, etc. in Greenland and Iceland, but also recorded from dogs in Denmark and China. It is 3 to 4 feet long, and distinguishable by its heart-shaped head and lack of an unsegmented neck (Fig. 100*D*). Its plerocercoids have been found in turbots in the Gulf of Finland. *D. parvum* is a small form reported in a few scattered instances in various parts of the world, believed by some helminthologists to be a dwarf form of *D. latum*. *D. houghtoni* occurs rarely in man, in China, and is found also in dogs and cats. It is 3 to 4 feet long and has a coiled rather than rosette type of uterus, and ellipsoidal eggs with rather pointed ends, smaller than those of *D. latum*; for a time it was thought to be *D. mansoni*. *Diplogonoporus grandis*, found 6 times in Japanese, is a huge worm, reaching a length of 15 to over 30 feet, with a width of 15 to 25 mm. The segments are 15 to 25 mm. broad and less than half a millimeter long, and have double sets of reproductive organs (Fig. 102*F*). Another species of the same genus, *D. brauni*, has been found in two Roumanians; it is only 12 cm. long and very indistinctly segmented. Probably it was not normally developed, man being an abnormal host. Other species of this genus are parasitic in seals and whales.

"*Sparganum*" Infections. — A larval worm known as *Sparganum mansoni* has been known as a parasite of man for many years. *Sparganum* is a group name for larval plerocercoids of unknown parentage. In 1917 Yamada and Yoshida obtained the adult by feeding larvæ from man to dogs; as previously suspected it proved to be a *Diphyllobothrium*. The whole life cycle was worked out by Okumura two years later.

The larval worm as found in man is a typical plerocercoid, much larger than that of *D. latum*, being from 3 to 14 inches in length (Fig. 108). It is a whitish, elastic, wrinkled worm with an invaginated scolex at the broader end. In man it is found in the muscles, subcutaneous connective tissue, or around the eye. The largest number of cases have been recorded from Indo-China, China and Japan, but scattered cases of this or closely related larvæ are known from almost every part of the world. Three cases recorded from Australia are believed by Cleland to be specifically distinct, and a case in East Africa has been named *Sparganum baxteri.* Other single cases have been found in British Guiana, Holland and Texas. The range of hosts in which the plerocercoid can develop is astonishing, and includes frogs, snakes, birds and mammals. Frogs and snakes, which are practically universally infected in the Far East, are commonly consumed by dogs and cats and their wild relatives, in which the adult *Diphyllobothrium* develops. The adults so far reared from human *Sparganum* cases are *D. mansoni,* but it is entirely likely that other species are also involved. *D. mansoni* is a smaller and more delicate worm than *D. latum,* 2 to 3 feet in length, with a coiled type of uterus and ellipsoidal eggs as in *D. houghtoni.* Human infection with the adults of this species appears not to be possible; the cases earlier recorded as *D. mansoni* were really *D. houghtoni.* The eggs of the worm, voided in the feces of the mammalian hosts, develop into procercoids in *Cyclops leuckarti,* and the second intermediate host ordinarily becomes infected by ingesting the cyclops, usually with drinking water. Many human infections in the Orient, however, seem to be acquired in a remarkable manner. Split fresh frogs are commonly used by the natives as a medical treatment for sore eyes and wounds, and when so applied the plerocercoids transfer themselves from the frogs to the human body. Faust experimentally transferred another species of *Diphyllobothrium* larvæ to dogs by applying them to the eyes as they would be applied by the use of medicinal frogs.

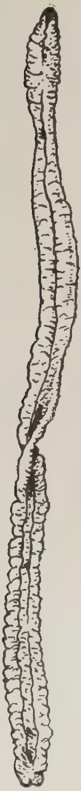

FIG. 108. *Sparganum mansoni;* nat. size. (After Ijima and Murata.)

Although Cram (1926) found *D. mansoni* in cats in Porto Rico, its main stronghold is in the Far East. It is quite likely that some of the cases of "*Sparganum mansoni*" from scattered parts of the world, and even in the Far East, are infections with other but related species of worms. Since the species cannot be determined without rearing the adults, it is better to refer to human infections with non-multiplying plerocercoids as merely "*Sparganum*" unless the adult is actually reared and identified, and it would seem wise to use Stiles' (1908) name "*Gatesius*" to distinguish the proliferating plerocercoids described in the next paragraph.

Another type of *Sparganum,* which has been termed *Sparganum*

(*Gatesius*) *proliferum*, was discovered by Ijima in a Japanese woman in 1904, and subsequently in three other Japanese cases and in one case in Florida. The worms are found by thousands, most of them in little oval tissue capsules 1 to 6 or 8 mm. long, appearing as acne-like nodules all over the skin, which may be badly swollen. They may be present in countless numbers not only in the subcutaneous tissue but all through the muscles and internal organs, including even the brain.

The worms (Fig. 109) are white, flattened organisms of very variable shape and size. They usually vary from 3 to 12 mm. in length, and from 0.3 mm. to 2.5 mm. in width, but in one Japanese case they were uniformly larger, reaching a length of three inches. Their peculiarly irregular shape is due to the unique method of proliferation by the growth of buds or supernumerary heads. These apparently become detached, leave the cyst, and become encapsuled themselves after migrating in the subcutaneous tissue. This explains the increasing numbers of acne-like spots or nodules containing worms.

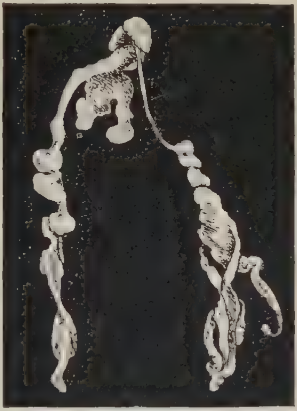

Fig. 109. *Sparganum proliferum*, from man in Florida. Much enlarged. (After Stiles.)

Attempts made by Ijima to produce adult worms by feeding the larvæ to various domestic animals failed, and nothing is known of the life history or mode of infection beyond a suspicion that the eating of raw fish is responsible for it. Dr. Gates, who discovered the Florida case, reported that there was probably a similar case in Florida a few years before, the patient having moved to California where he died "eaten up with worms."

The rare occurrence of this peculiar and serious parasitic disease is evidence that the mode of infection is unusual. The suspicion that it results from eating raw fish is sufficient reason for discrimination against this kind of food even in places where this or other human parasites which come from raw fish are not positively known to occur.

Order Cyclophyllidea. Family Tæniidæ

The vast majority of the tapeworms of mammals and birds belong to the order Cyclophyllidea which, as noted on p. 260, are distinguished by the presence of four in-cupped muscular suckers on the scolex, by having the yolk glands concentrated into a single mass near the ovary, and in having no mechanism for the exit of the eggs from the gravid uterus. The scolex, in addition to the suckers, very often has a protrusible "rostellum" at its tip, armed with one or more rows of hooks. The embryos remain passively in the egg or embryophore until eaten by the host in which it is to develop; this may be either a vertebrate or an invertebrate. In the case of one large family, the Anoplocephalidæ, which include many important tapeworms of herbivorous animals, the life cycle is still unknown. The larva may be either a cysticercus, a cœnurus, a hydatid, or a cysticercoid.

The family Tæniidæ includes for the most part relatively large worms, the majority of them parasitic in mammals. The rostellum is unarmed in a few species, but is usually provided with a row of powerful hooks, shaped as shown in Fig. 110; in most cases large and small ones alternate. The arrangement of organs in the proglottid is shown in Fig. 101. The uterus is in the form of a central stem from which lateral branched twigs grow out on either side, varying in number and appearance in the different species. The genital pores open at the edges of the segments, on irregularly alternating sides. The eggs (Fig. 65 *M* and *N*) are always recognizable; they have a very thin outer shell, sometimes provided with a pair of delicate filaments, which is ordinarily lost before the eggs are found in the feces, and the inner embryophore has a thick, brown shell which on surface view looks honeycombed, and in optical section looks striated. It is porous, and therefore fails to float in salt solution. The larvæ of most species are cysticerci, but in the genus *Multiceps* it is a cœnurus, and in *Echinococcus* a hydatid.

***Tænia solium* or Pork Tapeworm.** — This is a worm which is common in parts of the world where pork is eaten without thorough cooking, especially in some localities in Europe, but it is rare in the United States. In Jewish and Mohammedan countries where the eating of pork is a serious religious misdemeanor, this parasite has little chance of survival, and is scandalous evidence of moral turpitude when it does occur, just as is the beef tapeworm in Hindus. In spite of the rarity of human cases in America and also in the Philippines, the bladderworms are comparatively common in hogs; this fact has never been satisfactorily explained.

The pork tapeworm usually attains a length of 6 to 10 feet; records of specimens much longer than this are probably due to confusion of parts of more than one worm; there are 800 or 900 proglottids. The scolex is hardly larger than the head of a pin, about 1 mm. in diameter, and has a rostellum armed with from 22 to 32 hooks (Fig. 110, *B–E*), long ones (180 μ) and short ones (130 μ) alternating. Behind the head is a thin, unsegmented neck; the younger segments are broader than long, but in the middle part of the worm they become square, and the ripe ones are about twice as long as broad, shaped somewhat like pumpkin seeds, and about 12 mm. long. The sexually mature proglottids closely resemble those of *T. saginata* (Fig. 101). Soon after sexual maturity is reached and sperms for fertilizing the eggs have been received, the uterus begins to develop its lateral branches; in this species there are only from 7 to 10 main branches on each side, a fact which is of special value in distinguishing the ripe segments from those of *T. saginata*, which has about twice as many (Cf. Figs. 102 *A* and *B*). The fully ripe uterus usurps nearly the whole proglottid, while most of the other reproductive organs degenerate.

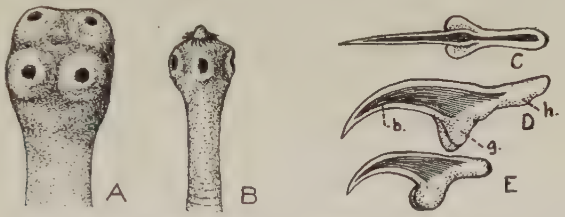

FIG. 110. *A*, "unarmed" scolex of *Tænia saginata; B*, "armed" scolex of *T. solium;* × 10. *C–E*, hooks of *T. solium*, much enlarged; *C*, long hook, dorsal view; *D*, long hook, lateral view; *E*, short hook, lateral view; *b.*, blade; *g.*, guard; *h.*, handle.

A man infested with a pork tapeworm expels ripe segments, singly or in short chains, almost every day. Several hundreds a month are cast off, each loaded with thousands of eggs. The thin outer shells are seldom seen; the thick, striated, brown embryophores are nearly spherical and measure 35 to 42 μ in diameter. Fortunately a majority of these never get an opportunity to develop further, but it is easy to see how some of them may reach their intermediate hosts, usually pigs, which are highly coprophagous, especially in the tropics. Aside from coprophagy, animals are exposed to infection from eggs scattered by rain and washed into drinking places, carried on the feet of flies, adhering to feet of man or animals, etc., and contaminating food or water. The filthy way in which hogs are usually housed and fed gives ample opportunity for their infection if the infested people are at all careless in their personal habits, or if privies are built in " open-back " style, or so that they leak. Young pigs are especially likely to become infected. Pigs are not, however, the only intermediate host; camels, dogs, monkeys and man can also serve as hosts for the bladderworms.

Upon ingestion by a suitable animal the oncospheres are liberated, bore through the intestinal wall, and make their way, via the blood or lymph channels, usually to the muscles or meat, but they may settle in almost any part of the body. They especially favor the tongue, neck, heart and shoulder muscles, and, next in order, certain muscles of the hams. Having arrived at their destination they grow into bladderworms or cysticerci, technically named *Cysticercus cellulosæ.* The bladders are small, oval, whitish bodies with an opalescent transparency, 6 to 18 mm. long (Fig. 103*D*), with a denser white spot on one side where the scolex is invaginated. Pork containing these larvæ is called "measly" pork. Sometimes they are so numerous as to occupy over one-half of the total volume of a piece of flesh, numbering several thousands to a pound.

When pork containing the bladderworms is eaten by man, all but the scolex is digested, and the latter, turning right side out and anchoring itself to the wall of the small intestine, grows to maturity in about two to three months. Man is the only animal known to serve as a final host, though considerable growth takes place in dogs.

The symptoms of infection and methods of treatment are described on pp. 262 and 263. This species is particularly dangerous because the bladderworms as well as the adult can develop in man; self-infection with the larvæ can result either from contaminated hands or by a reversal of the peristaltic movements of the intestine which throws the ripe proglottids of the worm back into the stomach, where the embryos in the eggs are liberated by the gastric juice. A century ago 2% of the human autopsies in Berlin showed these cysticerci, but they are less common now because of reduction of pig infections and consequently of human infection with the adults. The effects produced by the cysticerci depend entirely on their location in the body. A few of them in the muscles or in the subcutaneous connective tissue is nothing to worry about, but they may create unpleasant disturbances when they locate in the eye, heart, spinal cord, brain or other delicate organs, chiefly as the result of mechanical pressure. Infection of the brain, which is frequent, may cause epileptic fits, convulsions, paralysis, etc. In the eye they may seriously interfere with vision. Diagnosis and treatment are difficult; results of treatment with male fern are contradictory, and surgical removal of the cysts, though sometimes feasible, is often impossible on account of the number and position of the parasites.

Tænia saginata **or Beef Tapeworm.** — This is the commonest large tapeworm of man. It has a world-wide distribution, and in some localities infects a very high percentage of individuals. In some localities in Africa and Syria, and also among Tibetans, for instance, one-fourth to one-half of the inhabitants are infected. The Tibetans prepare beef by broiling it in large chunks over an open fire; while this sears the surface it scarcely warms the interior. In the Hindu sections of India *T. saginata* is religiously ostracised, since only the foulest outcasts will eat the meat of the sacred cow or even of water buffalos.

The beef tapeworm ordinarily reaches a length of from 15 to 20 feet, but specimens up to 35 or 50 feet have been recorded; the proglottids of an average worm number 1000 or more. The scolex (Fig. 110*A*) is 1.5 to 2 mm. in diameter, and is unarmed, *i.e.*, entirely devoid of hooks. The mature and ripe proglottids (Figs. 101 and 102*A*) are larger than in *T. solium*; the terminal segments are 15 to 20 mm. in length, and only about one-third as wide when relaxed, but they are very active and capable of much contraction and expansion. The ripe segments can always be distinguished from those of *T. solium* by the presence of 15 to 20 or more main branches on either side of the uterus, which sub-branch and leave practically no space between them.

The detached ripe segments are commonly voided singly. The embryophores (Fig. 65*N*) are more oval than in *T. solium*, measuring 30 to 45 μ by 25 to 30 μ. The life cycle is practically identical with that of *T. solium* except that the intermediate hosts are usually cattle or allied animals. However, giraffes, llamas, and prong-horn antelopes are occasionally naturally infected, and lambs and kids have been experimentally infected. In Europe and America cattle are usually only lightly infected in contrast to the heavy infections with *T. solium* often present in pigs, but in the tropics, where cattle and buffaloes are habitually coprophagous, they often have their flesh thoroughly riddled by the cysticerci. In India cattle frequently follow human beings to the defecation sites in anticipation of a fecal meal. The cysticerci (named *Cysticercus bovis*) in measly beef are 7.5 to 10 mm. wide by 4 to 6 mm. long. They are most frequently present in the muscles of mastication and in the heart; these are the portions of the carcass usually examined in meat inspections. They are, however, not conspicuous and can easily be overlooked in raw or " rare " beef.

Other Species of *Tænia* and *Multiceps*. — The genus *Tænia* and the genus *Multiceps*, which is distinguishable only by the multiple heads produced in the larvæ, include many species which are parasitic as adults in dogs and cats, and as larvæ in herbivorous animals. Some of the commonest ones in dogs are *Tænia pisiformis*, the larvæ of which develop in the liver and mesenteries of rabbits; *T. ovis*, developing in the connective tissue in muscles of sheep; *T. hydatigena*, developing in the liver of sheep; *Multiceps multiceps*, (Fig. 111) developing as a cœnurus in the brain of ruminants and causing gid; and *M. serialis*, developing in subcutaneous connective tissue of rabbits. *T. pisiformis* and *T. hydatigena* occur also in cats, but the commonest form in these animals is *T. tæniæformis*, which develops in the livers of rats and mice into a bladderworm with a scolex which produces a considerable chain of undeveloped segments, and is sometimes called a strobilocercus. One of these species, *Multiceps multiceps*, has been recorded once, in a Paris locksmith, as a cœnurus in the human brain, giving rise to epilepsy and loss of memory. One other cœnurus, *Multiceps glomeratus*, was found once in the rib muscles of an African; it was originally discovered as a parasite of jumping mice (gerbilles). All the species of *Multiceps* have crowns of large hooks similar to those of *Tænia solium.*

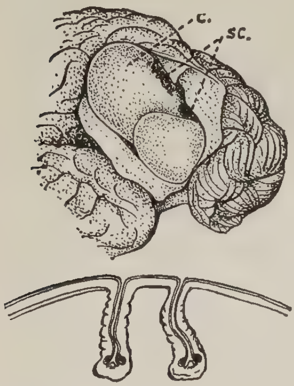

Fig. 111. Brain of "giddy" sheep with cœnurus (*c*), showing masses of scoleces (*sc*). Below, section of cyst wall showing invaginated scoleces. (After Neumann, from Hall.)

There are a few rare adult tæniæ which have been found in man. One is *Tænia confusa*, resembling *T. saginata*, but with larger and more elongate segments and minor anatomical differences. Four cases have been discovered in the United States, two in Nebraska, one in Texas and one in Louisiana; a worm described as *T. bremneri* from a Nigerian is probably the same species. Another species, of which two specimens were obtained from an East African, is *T. africana.* It has segments broader than long, an unarmed scolex, and a uterus with unbranched arms.

Echinococcus granulosus. — This is a minute species of tapeworm living as an adult in the intestines of dogs and allied animals. In contrast to its minute size as an adult it produces enormous larvæ known as hydatid cysts, which develop in many herbivorous animals and also in man.

The worm is found in the sheep and cattle-raising districts of the world, mostly outside of the tropics, especially Europe and North Africa, across north central Asia to Japan, Iceland, Philippines, southeast Australia and New Zealand, North America and southern South America. Human cases are especially common in Iceland, North Africa, Cape Colony, Victoria and Tasmania, and South America south of Brazil. In Iceland, at one time, from 4 to 16% of the human population was infected, but it is now much less frequent. In parts of South Australia more than 25% of the dogs are infected, and 2% of human beings. Sheep and cattle are very extensively infected in some of the endemic areas.

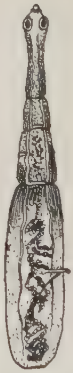

Fig. 112. *Echinococcus granulosus* from dog. × 10. (After Leuckart.)

The adult, (Fig. 112) though structurally very much like a *Tænia*, is very unlike one in size. It is only 3 to 6 mm. in length, and consists of a scolex and neck followed by only three or four successively larger segments, one immature, one or two mature, and usually one ripe or nearly ripe. The head has a very protrusible rostellum armed with a double row of 28 to 50 hooks. The worms occur by hundreds or even thousands in the intestines of dogs, but are usually overlooked on account of their minute size.

The development of the huge larvæ has been studied especially by Dévé, Dew, and more recently Cameron. The eggs are almost exactly like those of *T. saginata*. They are expelled free or in the ripe proglottids in the feces of dogs in pastures, and gain access to their usual sheep or cattle hosts with contaminated forage or water. Many other animals also become infected, including monkeys, all kinds of ruminants, carnivores, rabbits, horses, kangaroos, etc. Human infection usually results from contaminated water or from too intimate association with dogs; children are especially liable to infection by allowing dogs to " kiss " them or lick their faces with a tongue which, in view of the unclean habits of dogs, is an efficient means of transfer of tapeworm eggs. The liberated oncospheres enter the blood stream in the intestinal walls and are carried about until filtered out by capillaries through which they cannot pass. The first filter, and therefore the most frequent site of development, is the liver, and next to this the lungs. Fewer numbers reach the kidneys, spleen, intestinal walls, peritoneal lining, genital organs, heart, brain and various muscles.

Development of the cysts is slow. The young larva changes into a hollow bladder, around which the host adds an eveloping, fibrous cyst wall. At the end of a month these cysts measure only about one mm. in diameter; in five months they are about 10 mm. in diameter, and the inner surface is beginning to produce hollow brood capsules. These ultimately remain attached only by slender stalks, and often fall free into the fluid-filled cavity of the mother cyst. As the cyst grows larger more brood capsules form, and the older brood capsules begin to differentiate, on their inner walls, a number of scoleces, usually from 3 or 4 to 30 (Fig. 113). Sometimes the mother cyst, as the result of pressure, develops hernia-like buds which may separate off and continue their development independently, as daughter cysts. The fluid of the cysts is nearly colorless, and is composed of serum-like constituents which have permeated from the host, and from which the parasite absorbs its nourishment, and it also contains the waste products of the growing parasite; it has a granular deposit in it, consisting of liberated brood capsules and free scoleces; this is called " hydatid sand." Eventually such cysts commonly reach the size of an orange and may get as large as a child's head. One instance is recorded of an Australian with an abdominal cyst which contained 50 quarts of fluid. When their growth is unobstructed the cysts assume a more or less spherical shape, but are often deformed by pressure. When developing in bones, the cysts grow along the bony canals, often eroding the bone; daughter cysts are frequently formed in a hernia-like manner, when opportunity for escape from the cramped quarters is afforded.

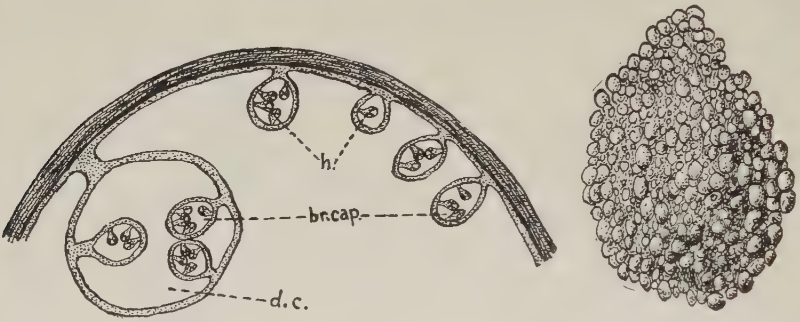

FIG. 113. Left, Diagram of portion of small hydatid cyst showing daughter cyst (*d.c.*), brood capsules (*br. cap.*), and invaginated heads or scoleces (*h.*) × about 5. Right, multilocular cyst from liver of steer, ⅔ nat. size. (After Ostertag from Stiles.)

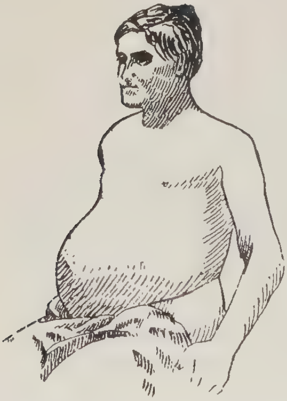

FIG. 114. *Echinococcus* cyst in liver of man. (After Huber from Stiles.)

Hydatid cysts grow persistently for years. In one recorded case a swelling had gradually developed during 43 years over a large portion of the face of a woman, and was as large as a child's head. When removed by an operation this was found to be a hydatid; such huge cysts are, however, exceptional.

Sometimes instead of forming single large vesicles, the development of the larva leads to the formation of a sponge-like, constantly growing mass of small separate vesicles imbedded in a fibrous tissue (Fig. 113). It is not delimited by a capsule formed by the host, and the vesicles contain a gelatinous substance instead of fluid. Roots grow out into neighboring tissues. The central portions degenerate and die while growth continues on the outside, as in a true malignant tumor. Often portions of the growth become separated and continue to grow like the parent; such detached portions may be carried by the blood-vessels to distant parts of the body. This type of cyst is known as a multilocular or alveolar hydatid cyst, and occurs principally in the liver, especially in parts of Europe. The fact that these dangerous growths are not known in Iceland or Australia where the ordinary unilocular cysts are so common, and are the predominant type in some European localities, has led to a belief by some parasitologists that they are caused by a different variety or species of *Echinococcus*, *E. multilocularis*, the adult of which may not be structurally distinguishable from *E. granulosus*. Others, however, think that the different effects are due to environmental conditions in the tissues of the host. In both types of cysts development is frequently imperfect and the parasite may fail in its life's work of producing scoleces which can grow into adults. Sometimes no brood capsules are formed, and in other cases the parasite succeeds in producing brood capsules but fails to form scoleces; such cysts are " sterile."

Hydatid cysts may cause serious disturbances by the pressure they exert on surrounding organs, with effects which vary, of course, according to the location of the cysts, but resemble those of slow-growing tumors. The liver of an ox containing hydatids has been known to reach ten times its normal size. When *Echinococcus* embryos get lodged in the brain or eye, the results are likely to be disastrous.

The hydatid fluid contains toxic substances, but normally these are kept localized by the fibrous wall by which the host imprisons the parasite; this is evident from the presence of eosinophiles only in the immediate vicinity of the cyst. If, however, the cyst " leaks," the toxins are distributed and eosinophilia becomes general. When the cysts are ruptured by pressure or injury, not only is the toxic fluid liberated, sometimes with serious results, but liberated brood capsules or other parts of the germinative layer of the parasite are scattered and may form new cysts in other parts of the body, especially if the primary cyst was located in the heart or ruptured into a large vessel. Multilocular cysts, which are not imprisoned by the host, are especially likely to produce secondary cysts.

Hydatid cysts are now usually diagnosed by serological methods, using fresh hydatid fluid as an antigen. Although precipitation and complement-fixation tests are possible, the so-called Casoni reaction, in which the skin of an infected individual responds in a characteristic manner to injection of filtered hydatid fluid, is easier and better. The older method of diagnosis by puncturing a cyst and withdrawing fluid in which scoleces are sought is dangerous, both on account of possible bacterial infection and risk of liberating hydatid fluid containing brood capsules, etc., which may produce toxic effects and also result in the formation of secondary cysts.

Treatment is purely surgical, but the parasite grows fast to the fibrous wall formed by the host and does not "shell out." It is dangerous to withdraw fluid directly, and it is customary to withdraw part of the fluid with a trocar, and replace it at once with a formalin or mercuric bichloride solution to kill the scoleces, brood capsules, etc. Subsequently the fluid can be drained out. Multilocular cysts can seldom be operated on successfully, and generally lead to death in a few years.

Prevention, aside from care with respect to too much intimacy with possibly infected dogs and careful washing of dishes from which they have eaten, consists in avoidance of food or water which might have been contaminated by dogs, and care that dogs are not fed, or do not get access to, the entrails or waste parts of slaughtered or dead animals from which they can become infected. A great reduction of the disease has occurred in Iceland as the result of a law controlling dogs by taxation and treatment, and enforcing the burial or burning of infected material.

Other Cyclophyllidea

Outside of the family Tæniidæ there is only one tapeworm commonly parasitic in man, namely *Hymenolepis nana*, but there are a considerable number of others which are more or less rare human parasites. The family Hymenolepididæ, of which *Hymenolepis* is the type genus, contains a very large number of species of tapeworms parasitic in birds and mammals, particularly in the former. They are small or medium sized worms, the heads of which are, with few exceptions, armed with a single row of hooks. The segments are relatively broad and are characterized by a very small number of testes (3 in *Hymenolepis*), and by a sac-like uterus which does not break up into individual egg balls. The larva is a cysticercoid which develops either in invertebrates or in the intestinal villi of the final host. Three species of this family have been found in man. Of these *H. nana* is a very common parasite of man and rodents; *H. diminuta*, abundant in rodents, is relatively rare in man, but by no means a curiosity; *H.* (*Drepanidotænia*) *lanceolata*, normally in ducks and geese, has been recorded in man once. The family Dipylidiidæ contains a number of species of the genus *Dipylidium*, found primarily in dogs and cats. They have a retractile rostellum armed with several rows of hooks shaped like rose thorns, a double set of reproductive organs, and a uterus which breaks up into numerous egg capsules. The larvæ are cysticercoids which develop in fleas or dog-lice. One species, *D. caninum*, has been found in man upwards of a hundred times. The family Anoplocephalidæ contains many important parasites of herbivorous animals, such as *Moniezia* and *Thysanosoma* in ruminants, *Anoplocephala* in horses, *Cittotænia* in rabbits, and *Bertiella* in primates and pigeons. In spite of the abundance and importance of these worms nothing whatever is known of their life cycles. They have unarmed heads, very broad and short proglottids, and either single or double sets of reproductive organs. The uterus is a transverse sac-like structure which develops out-pocketings or a reticular form. The eggs of most species have embryophores with peculiar horn-like processes known as the " pyriform apparatus." Of this family two species of the genus *Bertiella* have been found in man. The family Davaineidæ includes many species parasitic in birds, some of which are important pests of poultry, but a few live in mammals. The tapeworms of this family are peculiar in having the suckers on the scolex armed with rows of minute hooklets, as well as having two or three rows of smaller hammer-shaped hooklets on the rostellum. As in the Dipylidiidæ, the uterus breaks down into numerous egg capsules containing one or several eggs each, which nearly fill the ripe segments. In the few species in which the life cycle is known, the larvæ develop as cysticercoids in invertebrates. Three species have been found in man, all belonging to the genus *Raillietina,* formerly a part of the genus *Davainea;* they are *R. madagascariensis, R. formosana,* and *R. asiatica.* There are a number of other families of Cyclophyllidea but they have no representatives in man, and no important ones in domestic animals.

Hymenolepis nana. — The dwarf tapeworm, *Hymenolepis nana,* is the smallest adult tapeworm found in man, but it makes up for its diminutive size by the large numbers which are often present. It has a world-wide distribution, but is far commoner in some localities than in others. It is the commonest tapeworm in southern United States, where about one to two per cent of the population, especially children, are infected. In Europe it is especially common in Italy. In some parts of India as high as 18 to 28% of the population was found by the writer to be infected.

The adult worm (Fig. 115), consisting of 100 to 200 proglottids, is very variable in length, ranging from 7 to over 100 mm.; in general the length of the worms is inversely proportional to the number of worms present; in heavy infections it is commonly from 20 to 30 mm., with a maximum breadth of only 500 to 600 μ; it is so small and delicate that it resembles a strand of mucus in the feces, and therefore is seldom found after treatment, even when diligently searched for. The scolex (Fig. 116) has a well developed rostellum with a crown of 20 to 30 hooks. All the proglottids are considerably broader than long. The arrangement of the organs in mature proglottids can be seen in Fig. 116. The uterus develops as a sack with out-pocketings, and in ripe proglottids loses its form entirely, so that the whole segment between the longitudinal excretory vessels is solidly crammed with eggs.

The eggs have a very characteristic appearance (Fig. 115). The outer shells are usually oval and are thin and practically colorless; they commonly measure about 40 by 50 μ but may vary from 40 to 60 μ in length, or they may be spherical. The embryophore is lemon-shaped, 16 to 20 μ long, with a little knob at either end from which arise a number of long, delicate, wavy filaments which lie in the space between the embryophore and the outer shell.

The life cycle of the worm was long a matter of dispute, but it is now established that, unlike any other tapeworms except one or two others in the same genus, the entire development ordinarily takes place in one host. When the eggs are ingested, the oncospheres begin to claw actively inside their shells, and escape in the lumen of the intestine. They burrow into the interior of the villi, and there develop into typical cysticercoids in about four days (Fig. 117). On reaching maturity these make their way into the lumen of the intestine, the scoleces attach themselves, and the worms grow to maturity in about 20 to 30 days. Although this is the usual life cycle, Joyeux has found that this worm can still revert to the habits of its ancestors and develop in insects; he was able experimentally to get the cysticercoids to develop in adult grain beetles (*Tenebrio*), though with some difficulty. The cysticercoids required up to 18 days to mature.

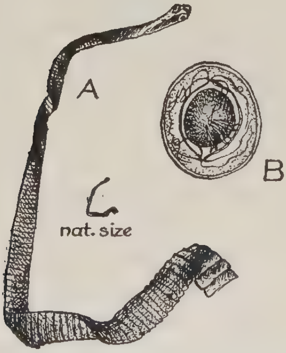

FIG. 115. *A*, dwarf tapeworm, *Hymenolepis nana*, × 7 (after Stein); *B*, egg of *H. nana*, × 700 (after Ransom).

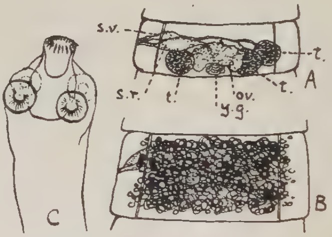

FIG. 116. *Hymenolepis nana; A*, mature segment; *B*, ripe segment; *C*, scolex; *ov.*, ovary; *s.r.*, seminal receptacle; *s.v.*, seminal vesicle; *t.*, testes; *y.g.*, yolk gland. Proglottids × 40, scolex × 75. (Original.)

There has also been much dispute as to the identity or otherwise of *H. nana* of man and *H. nana* of mice and rats. The human infection is relatively rare in some localities, especially northern Europe and Canada, where the rodent infections are common; in the warmer parts of the world rodent infections are still commoner, and human infections are frequent also. It has further been demonstrated that although eggs of human worms will develop in rodents and vice versa, this does not occur as readily as when the eggs are ingested by the same hosts as those from which the eggs were derived. The writer, however, got very strong epidemiological evidence in India to show that human infections are normally derived from eggs in the feces of infected rodents rather than from other human beings. The distribution of the infection in India is very irregular; in the flooded areas of eastern India, where ascaris and trichuris infections, which are acquired from eggs in human feces, are extremely common, *H. nana* infections are rare, while in the drier parts of central and northwest India ascaris and trichuris infections are rare and *H. nana* infections common. In other words, instead of there being any direct correlation between *H. nana* and infections known to depend on human fecal contamination, there is a practically perfect inverse correlation. On the other hand, the areas with common *H. nana* infections are those in which conditions favor an abundance of rats and mice in and about human habitations, and where the food habits are such as to lead to contamination of food by the droppings of these rodents. The correlation between *H. nana* infections and such rodent-borne infections as plague and *Hymenolepis diminuta* is in striking contrast to the inverse ratio of *H. nana* to ascaris and trichuris. The matter is one of considerable importance from the standpoint of control. The frequency of heavy infections is also an argument in favor of an important rôle of rodents in transmission, for while the accidental swallowing of a mouse "pill" with food could easily convey one or more whole segments of a worm with hundreds of eggs, such a wholesale contamination from human feces would be much less likely to occur. If, as the writer believes, human infection is commonly acquired from eggs derived from rodents, then the infection can be avoided by preventing access of rodents to human food which is to be eaten without further cooking, but if the infection is usually due to eggs derived from another infected human being, then sanitary measures will be found

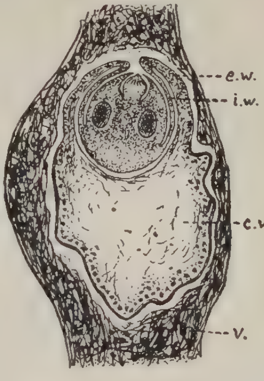

Fig. 117. Cysticercoid of a *Hymenolepis* (*H. erinacei*), nearly related to *H. nana*, in the villus of the intestine of a hedgehog; *c.v.*, caudal vesicle; *e.w.*, external wall; *i.w.*, internal wall; *v*, villus. × about 100. (After Joyeux.)

necessary. The effects of the infection, as well as treatment and diagnosis, have been discussed on page 263.

Other Species of *Hymenolepis*. — Man is also subject to infection with another rodent *Hymenolepis*, *H. diminuta*, which is very common in rats and mice in all parts of the world (Fig. 118). This is a much larger worm than *H. nana*, reaching a length of from 8 or 10 inches to 2 feet, with a maximum diameter of 3.5 to 4 mm. The head, unlike that of nearly all other species of *Hymenolepis*, is unarmed, and the segments are much broader than long. The structure of mature and ripe segments is very much like that of *H. nana*. The eggs are larger (60 to 80 μ in diameter), yellow or yellow-brown in color, and usually spherical. The oncosphere lacks the knob-like thickenings at the poles, or at best they are rudimentary, and there are no filaments.

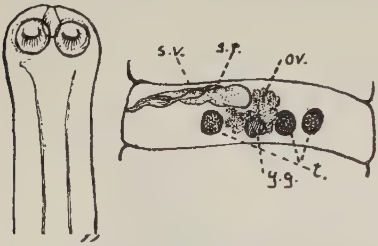

FIG. 118. Scolex and mature proglottid of *Hymenolepis diminuta;* proglottid × 8, scolex × 35; *ov.*, ovary; *s.v.*, seminal receptacle; *s.v.*, seminal vesicle; *t.*, testes; *y.g.*, yolk gland. (Original.)

Like most kinds of *Hymenolepis* this worm requires an intermediate host for the development of its cysticercoids; in this case the worm is satisfied with any one of many grain-infesting insects, including larvæ and adults of meal moths (*Pyralis farinalis*), nymphs and adults of ear-wigs (*Anisolabis annulipes*), adults of various grain beetles, such as *Tenebrio*, *Akis* and *Scaurus*, dung beetles (*Geotrupes*), cockroaches, the larvæ of fleas, and even myriapods. Joyeux (1920) considers the grain beetles, *Tenebrio molitor*, and rat fleas to be the usual intermediate hosts. When these insects are eaten the cysticercoids are liberated and the adult worms develop. Human infection results from eating such foods as dried fruits, pre-cooked breakfast cereals, etc., which are eaten unheated and in which the grain insects, infected from rat or mouse droppings, are present. Until recently this infection was considered sufficiently rare in man so that every instance was published as an incident worthy of note, but the writer found 23 cases in about 10,000 fecal examinations in India, and found no less than 3 in 50 examinations in one locality where the food habits and rat population were particularly favorable. As is usually the case with human tapeworms which belong in another host, this worm is very easily expelled after anthelmintic treatment, and is sometimes expelled spontaneously or after a cathartic.

The single record of human infection with another species, *Hymenolepis* (*Drepanidotœnia*) *lanceolata* occurred in Germany. This is a short stumpy worm, 4 to 13 cm. long, which widens out to from 5 to 18 mm.;

it is normally parasitic in ducks and related birds. The head has 8 hooks, and the proglottids are much broader than long. The intermediate hosts are water fleas or copepods. Probably this case resulted from the accidental ingestion of infected copepods with drinking water.

Dipylidium caninum. — This tapeworm (Fig. 119) is very common in dogs and cats and their wild relatives in all parts of the world, and over 100 human cases, nearly all in children, are known. It is a delicately built tapeworm, commonly reaching a length of about a foot. The head is very distinctive; it is prominently set off from the slender neck, and is provided with a rostellum which can be withdrawn into a sheath-like cavity, and which is armed with three or four rows of spines shaped like rose thorns. The mature and ripe proglottids are shaped like elongated pumpkin seeds, and are distinguished by having a double set of reproductive organs and a genital pore near the middle of each side (see Fig. 119). In living specimens the terminal segments have a pinkish or reddish color. The uterus develops first as a honeycomb-like network, and subsequently divides into numerous separate nests containing groups of eggs; each such "egg ball" contains from 5 to 15 or 20 eggs, and the eggs remain in the packets even when the segments disintegrate.

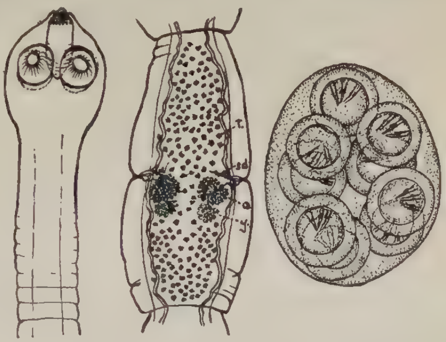

FIG. 119. Scolex (× 35), mature proglottid (× 11) and egg ball (× 180) of *Dipylidium caninum.* Note double ovaries, yolk glands and genital pores; *o*, ovary; *y*, yolk gland; *s.d.*, sperm duct; *t.*, testis.

The intermediate hosts are fleas (*Ctenocephalus* and *Pulex*), and also dog lice (*Trichodectes canis*). Joyeux (1920) observed that the eggs could not be ingested by adult fleas, but were devoured by the larvæ when preying on bits of fecal débris or disintegrating segments. After ingestion by a flea larva the embryos hatch in the intestine and bore through into the body cavity, where they remain very little changed until the flea has gone through its pupal stage and transformed into an adult. The *Dipylidium* embryo then proceeds with its development into a cysticercoid, which infects the final host when the flea is nipped. Children are infected while playing with dogs, probably by accidentally swallowing lice or fleas, by crushing them and then putting infected fingers into the mouth, or by having their faces licked by a dog just after the dog has nipped a flea. Most of the human cases have been discovered in Europe. There are a number of other tapeworms of the same genus found in dogs and cats, and it is altogether likely that these, too, can infect children if opportunity is afforded.

Bertiella. — At least two of the tapeworms of this genus which are apparently normally parasites of apes or monkeys can develop in man. One, *B. satyri*, was found once in a child in Mauritius and once in a child in Bengal; it has also been found in various apes at different points around the shores of the Indian Ocean. It attains a length of 10 or 12 inches with a maximum diameter of 10 to 15 mm., and is exceptionally thick and opaque. The head is unarmed, and the organs of the mature segments are arranged as shown in Fig. 120. The very broad ripe proglottids, less than a millimeter in length, and crowded with eggs provided with a "pyriform apparatus," are shed in blocks of 20 or more. A closely similar species, *B. mucronata*, originally found in a Paraguayan "howler" monkey, and subsequently in monkeys in a zoölogical garden in Cairo, Egypt, has been recorded by Cram (1928) from three young chimpanzees and a man in Cuba.

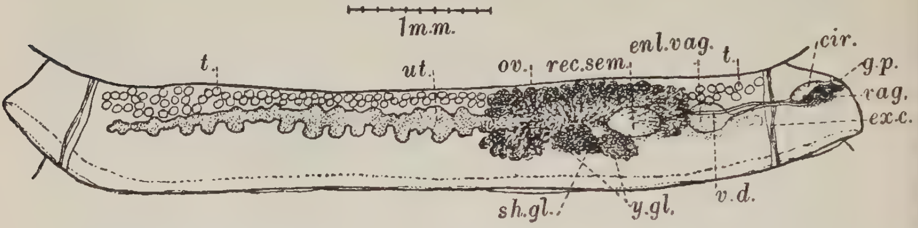

FIG. 120. Mature proglottid of *Bertiella satyri; cir.*, cirrus pouch; *enl. vag.*, enlargement of vagina; *ex.c.*, excretory canal; *g.p.*, genital pore; *ov.*, ovary; *rec. sem.*, receptaculum seminis; *sh. gl.*, shell gland; *t.*, testes; *ut.*, uterus; *vag.*, vagina; *v.d.*, vas deferens; *y.gl.*, yolk gland.

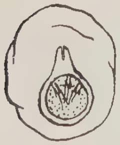

FIG. 121. Egg of *Bertiella satyri*, showing "pyriform apparatus." ×335 (Adapted from Blanchard.)

Although there is no certainty as to where the man got his infection, he had resided in Cuba for ten years, but no connection whatever could be traced between him and the chimpanzees. Cram calls attention to the danger there exists of establishing foreign species of worms in man or animals after introducing them with captive animals; it would appear that it might be important to examine imported animals for parasites just as imported shrubbery is examined for insects. In this connection Cram cites the case of a new parasite harbored commonly by rats in the vicinity of a zoölogical garden and not found in them elsewhere. Evidently the rats had acquired it from some animal in the garden, but in time it might become a widespread rat parasite. It is obvious that parasites of man or domestic animals could be brought in in a similar manner, providing a suitable intermediate host, if required, happens to be present.

***Raillietina* (*Davainea*).** — The three species of this genus which have been found in man are all rare human parasites, and their normal hosts are unknown. *R. madagascariensis* (Fig. 122) has been found ten times, nearly always in children, on islands, seaports or ships in the Indian Ocean off the east coast of Africa, and once each in the Philippines and Siam, but there is also one case from British Guiana. This slender worm is about 10 to 12 inches long with a maximum diameter of less than 1.5 mm. The ripe proglottids are about twice as long as broad. The eggs, several of which are enclosed in each of the 120 to 150 capsules, are elongate and more or less spindle-shaped. It has been suggested that the intermediate host, so far unknown, may be the ubiquitous seagoing cockroach. Another species, *R. formosana*, has been found by Akashi in children in Formosa and Tokyo; it is larger, has more numerous egg masses in the ripe proglottids, has larger eggs, and is said to lack hooks on the suckers. One other species, found once in Persia, has been named *R. asiatica*. The head was not found and the worm is very imperfectly described. It is evident that these worms, which undoubtedly utilize insects as intermediate hosts, as do the better known species of *Raillietina* in poultry, are capable of developing in man, but must very infrequently have an opportunity of doing so.

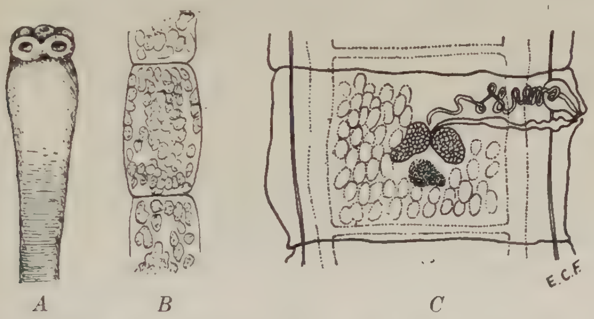

FIG. 122. *Davainea madagascariensis;* *A*, head and neck (× 8), after Blanchard; *B*, gravid proglottids, after Daniels; *C*, mature proglottid (× 24), adapted by Faust from Garrison.

CHAPTER XIV

THE NEMATODES IN GENERAL

The nematodes constitute a large group of worms of comparatively simple organization, nearly all of which are total strangers to everyone but zoölogists, and yet they play extremely important rôles in world economy. Popular ignorance of these animals is, as Cobb has remarked, easy to understand since they are seldom if ever seen; they do not supply food, raiment or other valuable material; they are not ornamental; they do not delight our ears with their songs, or otherwise amuse us; and they fail even to furnish us with classic examples of industriousness, providence, or other virtues, although they might well be extolled by "large family" enthusiasts. Thus avoiding the popular limelight, they do, nevertheless, unobtrusively leave their marks in the world. Probably every species of vertebrate animal in the world harbors nematode parasites in its body, and the majority of human beings on the earth fail to get through life without affording food and shelter for one or more species of them. About 50 different species have been recorded as living in the human body, and about a dozen of these are common human parasites, some of which cause diseases which are of prime importance to the human race. In addition to this the soil of our farms and gardens is literally teeming with myriads of nematodes, some of which do inestimable damage to crops. As compared with these the parasitic nematodes, with which we are concerned, constitute a mere handful, both of species and individuals.

The nematodes as a whole, while forming a well-defined group, show so little relationship to any other group in the Animal Kingdom that their affinities are a matter of pure speculation.

General Structure and Physiology. — The true nematodes are worms of comparatively simple organization. Probably the most primitive forms are to be sought among the free-living species which inhabit soil and water. The majority of the parasitic species are relatively giants, and are often much modified by their parasitic life. The free-living forms are at most barely visible to the naked eye, are transparent enough so that every structure in the body can be seen and its movements watched, and have extremely simple life cycles, whereas the parasitic ones, with a very few exceptions, are much larger, some of them up to several feet in length, are opaque, and may have relatively complex life cycles. There is no doubt but that certain free-living nematodes, or "nemas" as they are often called, are the most nearly like the ancestors from which all modern nematodes have come, but it is the general opinion that the parasitic forms do not represent a single line of development from which the various modern types have branched off in the course of evolution, but that the various modern types, first regarded as families, then superfamilies, and now as suborders or orders, arose entirely separately from different free-living ancestors. This, of course, makes their classification into major groups a matter fraught with difficulty, on which there is much difference of opinion.

A typical nematode is an elongated, cylindrical worm, tapering more or less at head and tail ends, and encased in a very tough and impermeable, transparent or semi-transparent cuticle which is of chitinous nature.

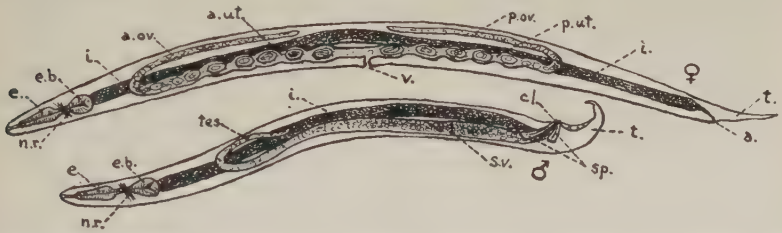

Fig. 123. Diagram of structure of a simple free-living nematode of *Rhabditis* type, ♀ (female) and ♂ (male): —*a*, anus; *a.ov.*, anterior ovary; *a.ut.*, anterior uterus; *cl.*, cloaca; *e.*, esophagus; *e.b.*, esophageal bulb; *i.*, intestine; *n.r.*, nerve ring; *p.ov.*, posterior ovary; *p.ut.*, posterior uterus; *sp.*, spicules; *s.v.*, seminal vesicle and sperm duct; *t.*, tail; *tes.*, testis. (Original.)

Usually the cuticle is marked externally by fine transverse lines called striations, and may have other inconspicuous markings, and sometimes bristles, spines, ridges or expansions of various kinds. In some parasitic forms there are such fin-like expansions in the neck region, in others in the tail region of the males, the latter commonly supported by fleshy papillæ; they are known respectively as cervical and caudal alæ. In the Strongylata there is a bell-shaped expansion at the posterior end of the males supported by fleshy rays conforming in number and arrangement to a definite plan; this is called a bursa. The cuticle is secreted by a protoplasmic "syncytial" layer in which no separate cells can be distinguished, though there are many nuclei. On the mid-dorsal, mid-ventral and lateral regions this layer is thickened into four "lines"; in the dorsal and ventral ones run the main nerve fibers, while in the lateral ones are smaller nerve fibers and the so-called excretory tubes. Between the "lines" there is a single layer of longitudinal muscle cells of very peculiar structure. The individual cells in cross section appear flask-shaped, the narrow outer part, adjoining the cuticle, having thick, striated contractile walls, while the inner part expands into a thin-walled protoplasmic bulb containing the nucleus. In large worms there are many such cells in a single layer in each quadrant of the body (Fig. 124), but in small worms there are only two muscle cells in a single cross section of each quadrant, and these are rhomboidal instead of flask-like in shape; these two types of musculature are called polymyarian (many-muscled) and meromyarian (few-muscled), respectively. The contraction of these muscles causes a twisting or bending of the body. There may be other special muscles in the esophagus, for moving the spicules, in the ovejector, etc.

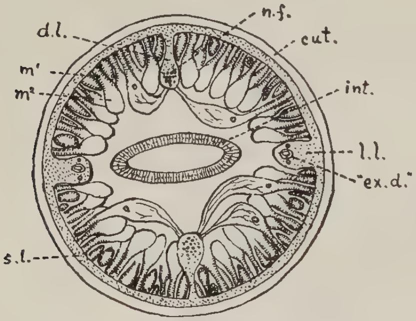

FIG. 124. Cross section of Ascaris, a polymyarian nematode; *cut.*, cuticle; *d.l.*, dorsal line; "*ex.d.*", so-called excretory duct; *int.*, intestine; *l.l.*, lateral line; m^1., striated contractile portion of muscle cell; m^2, protoplasmic portion of muscle cell; *n.f.*, nerve fibers. (After Brandes, adapted from Fantham, Stephens and Theobald.)

Between the muscles and the gut-wall there is a relatively spacious body cavity in which the reproductive organs lie, unattached except at their external openings. This cavity is not lined by an epithelium as is a true celome. It contains a fluid which serves as a distributing medium for digested food and for collection of waste products.

The nervous system consists of a conspicuous "nerve-ring" around the esophagus, from which longitudinal nerve trunks run forward and backward. Excretion, according to Mueller (1929) takes place through the body wall. Hitherto an excretory function has been assigned to the tubes which lie in the lateral lines of such worms as ascaris. These tubes are connected in the esophageal region by a "bridge," from which a single fine tube leads to a ventral external opening called the "excretory pore." In free-living nematodes the system consists of a single-celled gland-like organ likewise opening by an "excretory pore." Mueller could find no evidence whatever of an excretory function of this system, and thinks it highly unlikely that an excretory system would open in the immediate vicinity of the mouth, as it does in some species, where the excreted wastes would flow right back into the mouth. He is convinced that the "excretory system" really secretes a substance which is of use in the economy of the worm, and in the case of some species it seems evident that the secretion is salivary in nature. There is no circulatory system, and respiration takes place through the cuticle or possibly through the alimentary canal.

The mouth is variously modified. Baylis (1926) thinks that the most primitive form of mouth is a simple opening surrounded by three lips, one dorsal and two latero-ventral. This is the primitive type in free-living nematodes and is retained by many groups of parasitic forms, including *Strongyloides*, oxyurids, and ascarids, and their relatives in their several groups; for this reason Baylis includes all these in one great order "Ascaroidea," but has not been followed by other helminthologists. In some forms, *e.g.*, the filariæ and their allies, the lips have disappeared, while in others two lateral lips, sometimes with a dorsal and ventral one also, have replaced the primitive three. In still others, especially some of the Strongylata, the mouth has been highly modified into a " buccal capsule " which may be supplied with such modifications as crowns of leaf-like processes, cutting ridges, teeth, lancets, etc

The mouth, or buccal capsule, leads into the digestive canal. This is a simple tube leading from the anterior mouth to an anus usually a short distance from the posterior end. There are no accessory glands, and usually there are only two parts of the canal, an esophagus and an intestine. The esophagus in one order (Trichosyringata) consists of a single row of cells perforated by a fine canal, while in the other order (Myosyringata) it is surrounded by a wall which is either all muscular or partly muscular and partly glandular. Sometimes the posterior end of the esophagus enlarges into a bulb provided with valves. In any case the esophagus is separated from the intestine by tight-closing valves. The intestine is a flat or cylindrical tube, usually straight, lined only by an epithelium. At the posterior end it becomes chitinized as a rectum. In females the intestine has a separate anal opening, but in the males the intestine and reproductive system open into a common cloaca.

The organization of the Acanthocephala is totally different. The body, encased in a nematode-like cuticle, is provided at the anterior end with a proboscis armed with rows of recurved hooks, which can be withdrawn into a proboscis sheath. There is no vestige of a digestive tract. At the sides of the proboscis sheath is a pair of long tubular organs called lemnisci, of unknown function. The spacious body cavity contains the male or female reproductive organs, as the case may be, both opening at the posterior end of the body. The males have a pair of testes, one behind the other, and a vas deferens surrounded by a group of " prostate glands," opening into a bell-shaped invaginated " bursa " at the posterior end of the body. The females have a pair of ovaries in the larval stage, but these soon divide into many groups of multiplying cells which are free in the body cavity, and eventually fill it with eggs. These are drawn by a peculiar mechanism into a " uterine bell " and vagina, the latter opening at the posterior end of the body.

Development and Life Cycle. — The state of development of the freshly deposited eggs of nematodes varies greatly. In many they are still in the single-celled stage when deposited; in others they are in various stages from a few cells to fully formed embryos ready to hatch; and in still others they hatch while still in the uterus of the mother. Zawadowsky and Schalimov (1929) conclude that the degree of development of the eggs is determined by variations in the oxygen requirements for development. Eggs of ascaris and trichuris, for instance, will not develop at all without free oxygen; eggs of hookworms, oxyurids, etc., develop partially without free oxygen; while eggs of *Strongyloides*, trichina, filariæ, etc., develop to fully formed embryos without atmospheric oxygen, perhaps deriving this substance from oxygenated blood with which they are in fairly intimate contact. The egg cell segments into 2, 4, 8, 16, etc., cells, until it forms a solid morula. This then begins to assume a tadpole shape and becomes hollow inside, and then proceeds to form an elongated embryo provided with a simple digestive tract, usually with a bulbed esophagus like that present in many adult free-living species. The worm normally moults four times during the course of its development, but the successive stages, while differing in details of structure, are never totally unlike each other.

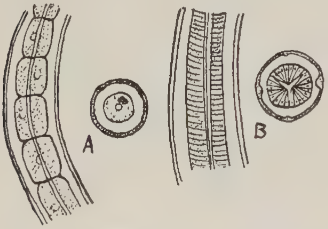

Fig. 125. Diagram of structure of esophagus of trichosyringate (*A*) and myosyringate (*B*) nematodes, in longitudinal and cross section. (Original.)

With rare exceptions parasitic nematodes have separate sexes, which are externally distinguishable; usually the males are smaller, and they differ in the form of the tail. In one instance the male lives as a parasite in the vagina of the female! In both sexes the reproductive system consists primitively of long tubules part of which serve as ovaries or testes and part as ducts. In all parasitic nematodes the male system is reduced to a single tubule, but the female system is double with rare exceptions, and in a few cases is further reduplicated. The inner ends of the tubules are fine, coiled thread-like organs closed at the ends, which produce the cells which ultimately becomes eggs or sperms. These sex glands open directly into a continuous part of the same tube which is larger in caliber and is called the uterus or vas deferens, as the case may be. The walls of the uterus appear to supply the yolk and shell-material for the egg. In the male the single vas deferens usually has an enlargement or seminal vesicle, and then opens into a muscular ejaculatory duct which opens into the cloaca. Male nematodes normally have a pair of chitinous " spicules," which lie in pouches beside the ejaculatory duct near the cloaca, and are capable of exsertion, to guide the sperms into the vagina of the female at the time of copulation. There may be a third smaller chitinous body or accessory piece called a gubernaculum. The size and shape of the spicules varies astonishingly in different kinds of nematodes, and is often very useful in identification. In a few cases one or both spicules may be missing. In the females of simple types of nematodes the two uteri come together near the middle of the body, and open into a single vulva. In most parasitic forms, however, the uteri first unite into a common tube, the vagina. Frequently the vagina, or the branches of the uteri, have enlarged thin-walled chambers which serve as seminal receptacles, and also muscular " ovejectors " which by a peristaltic muscular action force the eggs through to the vulva one at a time. The vulva, in different species, may vary in position from just behind the mouth to a point just in front of the anus.

The simplest type of life cycle is that in which the eggs are swallowed by the host, and direct development to maturity takes place in the intestine, *e.g.*, *Oxyuris* and *Trichuris.* This may be modified by a preliminary journey through the host's body, via heart, lungs, trachea and esophagus, and thus back to the intestine, *e.g.*, *Ascaris*, or by this and a preliminary partial development as a free-living larva outside the body, *e.g.*, hookworms. *Strongyloides* produces its eggs or embryos parthenogenetically, as there are no parasitic males, and may intercalate a generation of morphologically different free-living males and females. Trichina worms produce embryos which enter the host's body and encyst in the muscles to await being eaten by another host, thus substituting the original host for the outside world as a place for preliminary partial development. The filariæ and their allies (suborder Spirurata) substitute insects or other invertebrates as a place for partial development, thus requiring a true intermediate host. This is also true of the Acanthocephala, but in these the larva does not even remotely resemble the parent. The methods of escaping from and re-entering the final host vary in accordance with these various modifications of the life cycle.

Classification. — In recent years the process of promoting nematode groups to higher rank has gone on rapidly, and the families of a few years ago are now superfamilies, suborders or orders, according to the willingness of helminthologists to recognize the promotions. Thus Yorke and Maplestone (1926) recognize eight superfamilies, but Baylis and Daubney, the same year, combine some of these and come out with five orders. Cram (1927) divides the class into two orders and then, combining three of Yorke and Maplestone's superfamilies, comes out with a total of six suborders. In their respective books on helminthology or parasitology Baylis (1928) and Hegner, Root and Augustine (1929) follow Baylis and Daubney, while Faust (1929) follows Cram. The latter classification is accepted here, and is as follows:

Class Nematoda.

- *I. Order Trichosyringata.* Esophagus a fine capillary tube running through the center of a single row of cells; females with only one ovary; males with only one spicule or none at all.
  - 1. *Suborder Trichinellata (or Trichurata).* Includes trichina worms and whip-worms.
- *II. Order Myosyringata.* Esophagus surrounded by muscular, or muscular and glandular, cells.
  - 1. *Suborder Rhabdiasata.* Parasitic generation of parthenogenetic females only, the offspring of which give rise, under favorable conditions, to free-living males and females. Structure of latter like many free-living species. Includes *Strongyloides.*
  - 2. *Suborder Oxyurata.* Meromyarian (see p. 290); males usually with one spicule or none; eggs flattened on one side; mouth surrounded by 3 or 6 inconspicuous lips; esophagus muscular with a posterior bulb; tail of female usually slender and pointed. Includes pinworms.
  - 3. *Suborder Ascaridata.* Polymyarian (see p. 290); mouth typically with three lips; males with two (rarely one) spicules and usually with a slightly curled tail without caudal alæ; body usually large and relatively stout; esophagus muscular with or without a bulb. Includes *Ascaris.*
  - 4. *Suborder Strongylata.* Usually meromyarian; males with two spicules and with a true bursa supported by 6 paired rays, and one dorsal one which may be divided; mouth simple, without lips, or with a buccal capsule; esophagus muscular, without bulb; eggs thin-shelled and colorless. Includes hookworms, trichostrongyles, etc.
  - 5. *Suborder Spirurata.* Body usually long and slender; mouth either simple, without lips, or with two or four paired lips; esophagus slender, without bulb; males usually with 2 spicules, and coiled tail often with caudal alæ and papillæ; life cycle involves an intermediate host; often parasitic outside the alimentary canal. Includes filariæ, gnathostomes, *Gongylonema,* etc.

Class Acanthocephala.

Divided into three orders which, however, need not be considered here.

CHAPTER XV

TRICHINELLA, TRICHURIS, AND THEIR ALLIES

(SUBORDER TRICHINELLATA)

The worms belonging to the suborder Trichinellata differ so strikingly from all other nematodes in the form of the esophagus, which consists of a fine capillary tube pierced through a long column of single cells, that they are usually segregated into a separate order of their own, the Trichosyringata (meaning thread-throated). The anterior portion of the body, which contains only the capillary esophagus, is always very fine and slender, and in some forms is sharply demarcated from the relatively coarse posterior part of the body which contains the intestine and reproductive organs. The vulva opens either at the end of the esophagus or anterior to this point. In the species which produce eggs, the latter are very easily recognizable, since they are more or less barrel-shaped with an opercular plug at each end. *Trichinella*, however, produces no egg shells, and the embryos hatch before birth.

Trichuris or Whip-worms

The whip-worm derives its name from its peculiar whip-like form; the thick posterior part of the body corresponds to the handle, while the slender, sharply-marked-off, thread-like anterior end, which is longer than the rest of the body, represents the lash. The name *Trichuris* means " thread-tail " and was given before it was recognized that the slender part was really a head and not a tail. Someone else more appropriately named the worm *Trichocephalus* (thread-head), but since the other name was given first it must be used, in spite of its reflection on the inaccurate observation of its originator.

Whip-worms are common inhabitants of the cecum and large intestine of many animals, including dogs, rodents, pigs, and all sorts of ruminants, as well as man and monkeys. Schwarz (1928) has concluded that the whip-worms of pig and man are identical, and the whip-worm commonly found in apes and monkeys is also the same species. The human species, *T. trichiura*, is one of the most common worms parasitic in man. It has a world-wide distribution, but is commoner in the moist parts of warm countries. It usually inhabits the cecum but occasionally establishes itself in the appendix or upper part of the large intestine. It buries its slender head in folds of the intestinal wall, occasionally threading it into the wall, or even through into the body cavity.

The whip-worm has a length of 30 to 50 mm., of which the delicate, filamentous esophageal portion occupies about three-fifths. The males are a little smaller than the females and can be distinguished by the curled tail end of the body. The male has a single long spicule, retractile into a sheath with a spiny, bulbous end. The vulva of the female is at the junction of the "lash" and "handle" parts of the body; the uterus contains numerous eggs. The latter (Fig. 126) are easily identifiable by their shape, opercular plugs, and brown color; they measure about 50 by 22 μ, and are unsegmented when they leave the host.

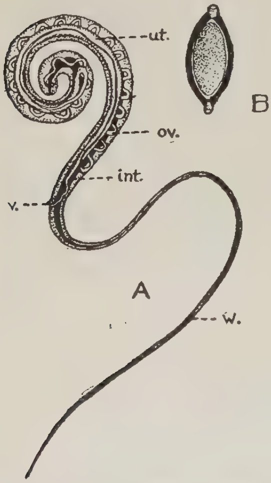

Fig. 126. Human whip-worm, *Trichuris trichiura: A*, female; *ov.*, ovary; *ut.*, uterus; *v.*, vulva; *int.*, intestine; *w.*, whiplike anterior end containing esophagus. × 3. *B*, egg; note barrel shape and pluglike bodies at ends, × 560.

The life cycle is very simple. The eggs develop slowly; even when kept moist and warm they require three to six weeks for the embryo to reach the hatching point, and under less favorable conditions they may be delayed for months or even years. Spindler (1929) has demonstrated experimentally that the eggs are less resistant to desiccation than are those of ascaris, and nearly all die within 12 days when dried on a slide, even in a saturated atmosphere. Epidemiological evidence shows that a high incidence of trichuris infection is always associated with conditions under which there is an abundance of moisture in the soil, due either to a heavy and well-distributed rainfall or to dense shade. Infection appears to result in some instances from polluted water, in others from contaminations, presumably via the hands and finger nails, from polluted moist soil. After ingestion the eggs hatch, usually if not always, according to Fulleborn, in the region of the cecum, and immediately attach themselves to the mucous membranes, without any attempt to migrate out of the intestine to go on a journey through the heart and lungs, as do ascaris larvæ. Fulleborn (1923) found no evidence of any burrowing, but Hasegawa (1924) states that the newly hatched larvæ enter the villi of the intestine and remain there for several days before taking up their residence in the cecum. In an experimental infection of himself by Calandruccio, eggs appeared in the feces about one month after infection.

Fortunately, since it is so common and is very difficult to get rid of, trichuris rarely does any evident damage to its host. Usually the only evidence of infection in man is the presence of eggs in the feces. Occasionally inflammatory processes develop when the worm pierces the intestinal wall with its slender head, and it may cause trouble when lodged in the appendix, by blocking it. Mild toxic symptoms may occasionally be present in heavily infected children. There is reason to believe that portals of entry are frequently made which may render the host more susceptible to bacterial infections, such as typhoid and dysentery, but the evidence against the worm is circumstantial and open to question. Heavy infections might be injurious, but these are rare in man. The writer recently saw an autopsy on a camel which died after several weeks of severe diarrhea; its large intestine contained unbelievable numbers of trichuris, which was the only pathological condition found.

On account of its position in the cecum, too far down the intestine to be reached in adequate concentration by anthelmintics given by mouth, and too far up to be reached by enemas, trichuris is a most difficult worm to expel. A proportion of them is usually expelled by such drugs as thymol, chenopodium and carbon tetrachloride, but complete " cures " are exceptional. Prevention, of course, consists in avoiding water or food which has been contaminated by the eggs.

There are a number of other worms related to trichuris found in various animals. A common one in rats is *Hepaticola hepaticola*, which lives in the liver and deposits its eggs in the liver tissue, where they accumulate and form characteristic, dry yellow spots. When an infected liver is eaten by another animal the eggs, already containing developed embryos, hatch and the larvæ reach the liver by way of the portal vein. One human case has been recorded in India, in a British soldier who died with a diseased liver, and three cases have been reported from Russia. It is probable that any savage tribes of men who eat rats would be in danger, and the infection would rarely if ever be diagnosed except at post-mortem. A closely related worm, *Eucoleus ærophilus*, inhabits the lungs and trachea of foxes, cats, etc. Numerous worms of the genus *Capillaria*, which are extremely fine and slender, occur in the intestines, and a few in the urinary bladder, of many kinds of vertebrates, but none have ever been found in man. Another related worm is *Trichosomoides*, found in the urinary bladder of rats; it is worthy of note because of the very inferior status of the males, which live permanently in the vagina or uterus of the females.

Trichina worms, *Trichinella spiralis*

The trichina worm, though an intestinal parasite as an adult, is quite different in significance from other intestinal worms. As far as the injuriousness of its presence in the intestine is concerned it is much less serious than many of the others, since its length of life as an adult is relatively short. The serious and often fatal results of trichina infection are due to the peculiar life history of the worm and are concerned with the offspring of the infecting worms and not with these worms themselves.

Structure and Life History. — The trichina worm, *Trichinella spiralis*, occurs in quite a large number of animals, but the readiness with which infection occurs in different species of animals varies greatly. In America hogs are most commonly infected, and infection is common in rats which have access to waste pork; in Europe dogs and cats commonly show a higher percentage of infection than hogs. Man is highly susceptible, in fact so susceptible that he cannot be considered a normal host of the parasite. Rats and mice are sometimes thought to be the primary hosts of the worm, but the fact that these rodents succumb easily to infection while the parasites are still in the intestinal stage tends to show that rats are not normal hosts. Rabbits and guinea-pigs are easily infected when fed meat containing the worms, and a number of other mammals can occasionally be infected artificially.

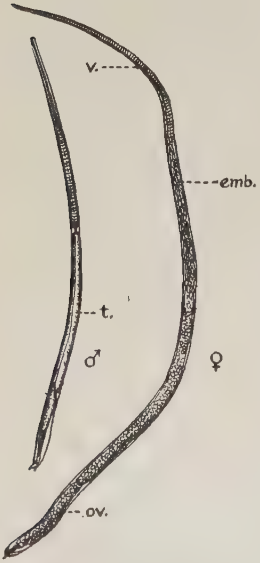

Fig. 127. Adult trichina worms, *Trichinella spiralis*, male (♂) and female (♀); *v.*, vulva; *emb.*, embryos in oviduct; *ov.*, ovary; *t.*, testis. × 25. (After Claus, from Braun.)

The worms gain entrance to the digestive tract as larvæ encysted in meat (Fig. 129). In the intestine of the host they are freed from their cysts and take refuge among the villi and folds of the mucous membrane of the small intestine. Here they mature and copulate as early as the third day after being swallowed. The female worms (Fig. 127) are from three to four mm. long, whitish in color, slender, and tapering from the middle of the body toward the anterior end; the males are only 1.5 mm. long. The long capillary esophagus occupies one-third to one-half the length of the body. In the female the vulva opens near the middle of the esophageal region, and the anterior part of the uterus is crowded with embryos, while the posterior part contains developing eggs. The males, aside from their minute size, are characterized by the presence of a pair of conical appendages at the posterior end. In both sexes, the anus (or cloaca) is terminal.

The adult intestinal worms are essentially short-lived, the males usually passing out of the intestine soon after mating, and the females as soon as they have given birth to all of their offspring. The adults usually disappear within two or three months after infection.

Trichina worms are peculiar in that they bring forth living young, free of the eggshell. They do not nourish their young within the body as do truly viviparous animals, but merely retain the eggs in the uterus until they hatch. Sometimes the young worms begin to be born within a week after the parents have been swallowed by the host. They are most numerous in the circulating blood between the eighth and 25th day after infection, though the greatest invasion occurs on the ninth and tenth days. When born they are scarcely 0.1 mm. in length. The mother worms usually burrow into the walls of the intestine far enough so that the young can be deposited directly into a lymph- or blood-vessel rather than into the lumen of the intestine. The larvæ are carried in the blood or lymph stream, and are distributed to nearly all parts of the body. They leave the capillaries in the striped muscles and penetrate into the fibers. Although young migrating larvæ may accidentally be carried to other tissues, and have even been found in the cerebrospinal fluid and in the mammary glands and milk of a nursing woman, they are apparently incapable of developing in any tissue except voluntary muscle. They may settle in the heart muscle, but degenerate there without continuing their development. The muscles particularly favored by the worms are those of the diaphragm, ribs, larynx, tongue and eye, which, as noted by Stäubli, are among the most active muscles and the muscles with the richest blood supply and largest amount of oxygen. According to Flury trichinæ have a high glycogen content, and probably subsist on the glycogen stored in the striped muscles; in fact the abundance of glycogen may account for their location in these muscles.

When the larvæ have arrived at their destination in the muscles they thread their way between the fibers towards the ends of the muscles (Fig. 128), ultimately penetrating the individual fibers where they coil up into loose spirals, constantly coiling and uncoiling as much as their close quarters will permit. When worms which are still boring are teased out of the flesh and warmed to blood heat, they can be seen constantly tightening and loosening their coiled form, reminding one of a fist being alternately clenched and unclenched. After entering muscle fibers the worms grow rapidly in size to a length of one mm., ten times their original size, and become sexually differentiated. The inflammation caused by the movements and waste products of the animals results in the degeneration of the enclosing muscle fibers and in the formation, beginning about a month after infection, of connective tissue cysts around the young worms. The cysts (Fig. 129), which are completely developed in from seven to nine weeks, are lemon-shaped, from 0.25 to 0.5 mm. long, lying parallel with the muscle fibers. As a rule only one or two worms are enclosed in a cyst but as many as seven in a cyst have been observed. When first formed the cysts are very delicate and can only be seen by careful focusing with the microscope, but they gradually grow thicker and more conspicuous, and after seven or eight months there begins a deposit of chalky calcareous matter (Fig. 130*A*). This process ultimately results in the entire cyst becoming hardened into a calcareous nodule (Figs. 130 *B* and *C*), and even the enclosed worm, which usually degenerates and dies after some months, becomes calcified after a number of years. There are cases, however, where the trichina worms do not die and disintegrate so soon, and the calcification process is much slower. There are records of these worms found living in cysts in hogs 11 years after infection and in man 25 to 31 years after, though it is doubtful whether in some of these cases a fresh

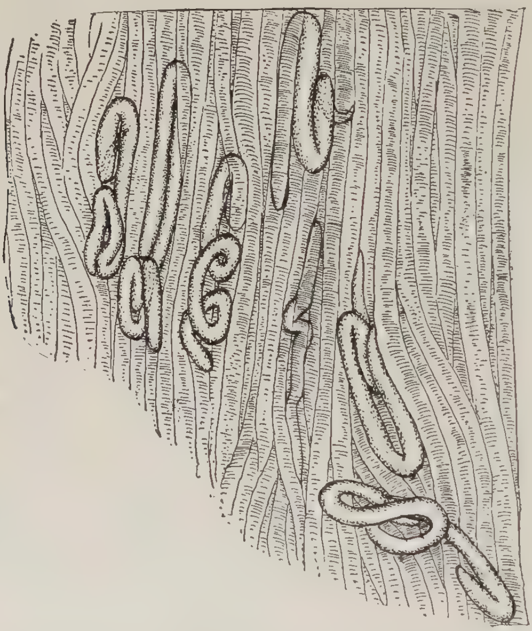

FIG. 128. Larvæ of trichina worms burrowing in human flesh before encystment. From preparation from diaphragm of victim of trichiniasis. × 75.

infection did not occur unknown to the patient or to the observers who made the records.

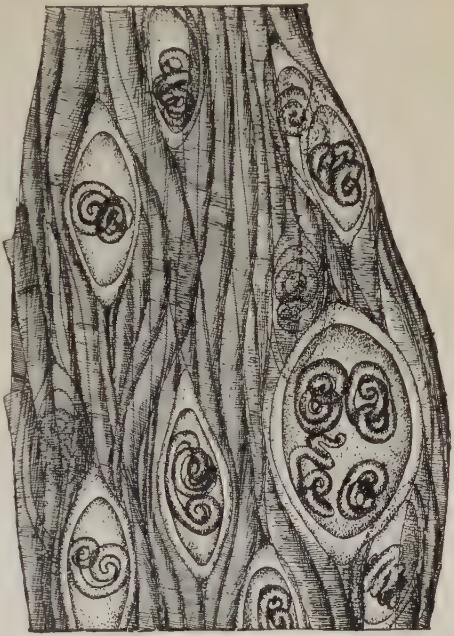

FIG. 129. Larvæ of trichina worms, *Trichinella spiralis*, encysted in striped muscle fibers in pork. Camera lucida drawing of cysts in infected sausage. × 75.

The larval worms, which, as pointed out by Ransom, on account of their advanced stage of development are comparable with the nymphs rather than the larvæ of arthropods, when encysted in the flesh of some susceptible animal never develop further until eaten by another susceptible animal. If they are eaten the cyst is dissolved off in the intestine of the new host, the larvæ are set free in the digestive tract, and within three days become sexually mature and copulate, to begin the performance all over. It is estimated that each female produces an average of 10,000 to 15,000 young. Since an ounce of sausage may contain over 100,000 encysted larvæ, most of which become females, the eating of this quantity of sausage may result in nearly one billion larvæ distributing themselves through the body of the unfortunate victim.

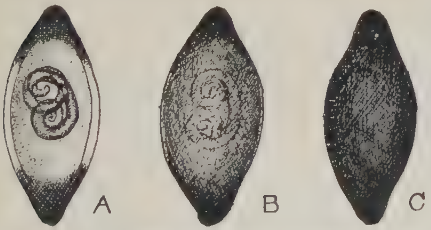

FIG. 130. Stages in calcification of trichina; *A*, ends calcified; *B*, thin layer of calcareous material over whole cyst, worm beginning to degenerate; *C*, complete calcification. (After Ostertag.)

Obviously man usually if not always becomes infected from eating infected pork, whereas hogs may be infected not only by eating scraps of raw pork but also by eating the bodies of infected rats and mice. The latter animals are infected in a similar manner. The number of trichina worms which may be harbored by a single host is almost incredible. According to the writer's investigations, the sausage which was the cause of an epidemic in Portland, Oregon, contained over

2,000,000 larvæ to the pound at a very conservative estimate, and in a bit of human muscle from the diaphragm of an Italian who fell victim to the disease the number of worms was even greater.

There can be little doubt but that this worm, with the pork tapeworm as an accomplice, was responsible for the old Jewish law against the eating of pork. It was, however, many thousands of years later, in A.D. 1828, that the worms were first discovered. A little over 50 years later, 1880–1891, the trichina worm was the cause of international complications between the United States and Germany, and during this time American pork was excluded from German markets on account of the alleged frequency with which it was found to be infected. The outcome of this trouble was the beginning of the present American system of government meat inspection.

Prevalence. — Since the danger of infection from eating imperfectly cooked pork has been given wide publicity, and has come about as near to being a matter of common knowledge as any fact of parasitology, the prevalence of the infection has been greatly reduced, but even now trichina embryos are found in from 0.5% to 2% of the inhabitants of most civilized countries, as shown by post mortem examinations. According to Ransom, statistics based on microscopic inspection of 8,000,000 hogs in the United States show only 1.41% infection with live trichina worms, and a total of 2.57% infection with live trichinæ and trichina-like bodies.

In some European countries the infection is somewhat less. Some of the great epidemics of trichiniasis (or trichinosis) in Europe have been attributed to American pork, but according to Ransom there have been no authentic cases of the disease in Europe from American pork up to recently, and, so far as known, none recently. Our slaughterhouses have been referred to as the great breeding centers of trichina, but this is true only as to slaughterhouses not under federal inspection.

The rôle of the rat in the spread of trichiniasis can readily be appreciated when the statistics concerning the infection of these animals in slaughterhouses, stables, etc., are examined. Of 51 rats captured in the Boston abattoir some years ago 39 (77%) were infected, and every one of 40 captured in a large exportation slaughterhouse in the same city was infected. Rats captured in stables where no hogs are kept, however, are usually less trichinized. Rats in localities where an epidemic of trichiniasis has recently swept through are usually extensively infected.

The prevalence of the disease in man is by no means parallel with its prevalence in other animals. The great controlling factor is the method of eating pork. Among such people as Americans, English and French, where pork is almost always eaten cooked, trichiniasis is rare and comes only from eating pork not *thoroughly* cooked, thus allowing a few worms to escape, though ordinarily not enough to cause serious disease. On the other hand very fatal epidemics have occurred among the Germans, Austrians and Italians, who are very fond of raw pork, especially in the form of sausage or " wurst." Nearly all the epidemics in America have been among the Germans or Italians who still cling to their native habits. The majority of all cases are reported as being caused by raw sausage or raw ham, and usually home-made or prepared in meat shops on a small scale. As stated by Ransom, " no cases of trichinosis have been reported which trace back to sausage prepared in establishments conducted on a large scale. While it is not impossible that such cases might occur, the chances seem very remote, for the reason that in such establishments any one lot of sausage is invariably made up of small portions from a large number of hogs, and the infection, if any be present among the hogs involved, is necessarily greatly diluted, with the result that no individual consuming the sausage is at all likely to ingest a sufficient number of trichinæ to produce an appreciable effect, even though the parasites should happen to survive the curing processes to which the commercially prepared sausage is usually subjected.

The Disease. — The disease caused by trichina worms is more fatal to man than to hogs, the fatality sometimes rising to 30% or more of the cases. Even in man the worms, if eaten only in small numbers, produce no serious or even noticeable effect. When eaten in great numbers, however, as would always happen in eating heavily-infected raw or under-done pork, the worms produce symptoms so much like typhoid fever that the disease is undoubtedly often diagnosed as such. The course of the disease, as described by Ransom, is somewhat as follows: the first symptoms of the disease — diarrhea, abdominal pains and intestinal catarrh — are the result of irritation of the intestine by the adult worms, especially the females, which burrow deep to deposit their young. Except in very light cases, a sort of general torpor is noticeable, accompanied by weakness, muscular twitching, etc. A very striking symptom, which appears in about a week and lasts for a few days, is a marked puffiness or edema of the face and especially of the eyelids. As pointed out by Ransom, the gravity of the case cannot be judged from the severity of the first symptoms. In some of the worst cases the first symptoms are very mild.

In nine or ten days or longer the second stage of the disease appears, accompanying the period of migration of the larvæ. This is the period which is frequently fatal. The most pronounced symptoms are intense muscular pains and rheumatic aches, with disturbances in the particular muscles invaded, interfering with the movements of the eyes, mastication, respiration, etc., the respiratory troubles becoming particularly severe in the fourth and fifth weeks of the disease, in fact sometimes so severe as to cause death from dyspnea or asthma. Profuse sweating and more or less constant fever, though sometimes occurring in the first stage also, are particularly characteristic of the second stage. The fever is commonly absent in children. The third stage, accompanying the encystment of the parasites, begins about six weeks after infection. The symptoms of the second stage become exaggerated, and in addition the face again becomes puffy, and the arms, legs and abdominal walls are also swollen. The patient becomes very anemic, skin eruptions occur, the muscular pains gradually subside and the swollen portions of the skin often scale off. Pneumonia is a common complication in the third stage.

Trichinella is unique among worms in causing constant fever. It is probable that the fever as well as certain changes in the blood corpuscles and chemical changes in the invaded muscles is due both to poisonous substances given off by the worms and to poisonous substances resulting from destroyed muscle tissue. Such substances have been found by Flury and Groll and others in cases of *Trichinella* infection. They are substances which act on the muscles themselves, on the nervous system, and on the blood-vessels. It is quite evident, as pointed out by Herrick, that with the invasion of the blood and tissues by millions of larvæ and with the breaking down of large amounts of muscle tissue a constant inoculation of the infected person with poisonous protein material is taking place, a condition which always gives rise to fever. Certain volatile acids are produced by the muscle degeneration, and these are considered by Flury to account for the muscular pains. Other toxic substances account for most of the other symptoms of the disease, *e.g.*, the marked increase in eosinophiles.

The duration and final outcome of the disease is variable, according to the heaviness of the infection. Death, as remarked before, may frequently result, and according to Ransom most commonly occurs from the fourth to the sixth week. It rarely occurs before the end of the second week or after the seventh. Recovery usually does not occur in less than from five to six weeks after infection, and often not for several months. Recurrent muscular pains and weakness may continue for years and a stiffness may persist indefinitely in the invaded muscles. Commonly cases in which a copious diarrhea appears early in the disease are of short duration and mild in type. Young children, due either to smaller quantities of pork eaten or to greater tendency to diarrhea, are likely to recover quickly.

Treatment and Prevention. — The search for a specific remedy for trichiniasis has so far been futile. Even the adult worms in the intestine are much more difficult to dislodge or destroy than are other intestinal worms, since they bore so deeply into the intestinal walls that the ordinary drugs do not affect them. Even were it possible to drive out the adults readily, this often could not be done in time to prevent disease or death, since the infection is seldom recognized before the larvæ are already produced and are migrating throughout the body. This is the critical stage of the disease; if the system can endure the irritation and inflammation produced by the burrowing of millions of worms and can withstand the effects of the toxins produced both from the worms themselves and from the destroyed tissues during the first and heaviest onslaught of the newly produced larvæ, the danger is past. The fever, the muscular pains, amounting to agony for a time, and the intestinal disorders continue for weeks but gradually subside. The treatment employed during all this time can only be symptomatic and of general nature — efforts to reduce the fever, to permit sleep, to keep the digestive system in as good order as possible and to do all that can be done to keep up the vitality and general health.

Diagnosis of trichina infections has hitherto been difficult, unless there were clear epidemiological clues. The clinical symptoms are not conclusive, though a combination of diarrhea, muscular pains and eosinophilia is suggestive enough to make a wide-awake practitioner inquire about pork-eating habits. During the intestinal phase of the disease careful examination of feces after purges or anthelmintics will usually reveal the minute adult worms, and later the larvæ can often be found in small excised bits of muscle, but it is then usually too late to be of much use. Bachman (1927) devised a method of isolating trichina larvæ from the meat of heavily infected animals; the larvæ thus obtained were made up into a powder which could be used as an antigen. In experimental animals it was possible to get reliable precipitin tests with this thirty days or more after infection, and Bachman later (1928) found that injection of his antigen, properly diluted, into the skin of infected animals produced typical reactions as early as four days after infection. This promises to be of considerable value in diagnosis.

Personal preventive measures against trichiniasis are easy and consist simply in abstinence from all pork which is not thoroughly cooked. Experiments by the U. S. Bureau of Animal Industry show that trichinæ are quickly destroyed by a temperature of 55° C. (131° F.), since the body protoplasm is coagulated at this temperature, but pork must be cooked for a length of time proportionate to its weight in order to insure the permeation of heat to the center. Experiments show that at least 30 to 36 minutes boiling should be allowed to each kilogram of meat ($2\frac{1}{4}$ lbs.). Hurried roasting does not destroy the parasites as long as red or raw portions are left in the center. Cold storage for 20 days or more at temperatures below 10° F. has been shown by Ransom to be destructive to trichinæ. The regulations of the U. S. Bureau of Animal Industry, relative to pork products customarily to be eaten without cooking, require freezing for 20 days at a temperature of not higher than 5° F., or curing in accordance with certain specified processes. Temperatures above 10° F. are more or less uncertain in their effects. Salting and smoking are not efficacious unless carried out under certain conditions. *Thorough* salting is effective, provided the meat is subsequently dried for about three weeks, whereas large pieces of pork placed in brine have been known to contain living trichinæ for over a month. Smoking as well as salting hastens the killing of the worms. Salt withdraws water from the parasites and renders them more susceptible to moderately high temperatures and to desiccation.

Prevention of trichiniasis by meat inspection methods is at best only partial, and, while meat inspection might help to lessen the chances of the disease, it should not be implicitly relied upon. Probably in an ordinary meat inspection all heavy infections would be found, provided the inspector has been doing his work properly. The inspection usually consists in the microscopic examination of a bit of muscle from tongue and diaphragm; if the examination is negative, the hog is passed. Obviously light infections must frequently escape notice, and the false sense of security which is the result of knowledge that meat has been "inspected" may do much damage. There is no inspection for trichinæ in force in the United States at the present time.

Much could be done to prevent the prevalence of trichina infection in pork by preventing hogs from eating food which might be infected. Hogs should never be allowed access to the carcasses of other hogs or to the dead bodies of rats and mice, or to waste scraps of pork. Dead hogs or waste pork, if there is any possibility of their being infected, should not be thrown where rats and mice could prey upon them. If these principles were carefully followed out, there is no doubt but that trichiniasis could be reduced to a much greater extent than it has been.

The symptoms of trichina disease in hogs are much less evident than in man, and there is no certain diagnosis of it in living animals except by microscopic examination of the muscles for the detection of the larvæ. When heavily infected, hogs show severe intestinal disorders, abdominal pains and stiff muscles, but there is nothing diagnostic in these symptoms. A farmer who drives sick hogs to market, however, in order to get rid of them, without giving proper warning of their condition which might make possible the discovery of trichina infection if present, should be considered guilty of criminal negligence, and punished in accordance with the damage done by this negligence. This is particularly true if he feeds his hogs waste containing raw meat, or allows them to feed upon dead animals — a very common practice.

As has recently been pointed out by Stiles, there is no practical or proper method of inspecting meat by which the absence of *Trichinella* can be guaranteed, and it is therefore unjust to hold a butcher responsible for cases of trichiniasis which may result from the eating of pork sold by him. There are laws which provide that " diseased meat " shall not be sold and that an implied warranty of fitness for food goes with any sale of food. Neither of these laws, however, can be unreasonably enforced. Technically *all* meat is diseased, since there are no market animals which are not parasitized in some way. As to the " implied warranty," this can go only with an implied guarantee on the part of the buyer that the food will be properly prepared before being eaten. Clams in the shell, unhusked corn and uncooked beans are guaranteed as being fit for food only when properly prepared. In like manner pork is sold with the understanding that it will be properly prepared, *i.e.*, thoroughly cooked. Raw pork, since it is likely to contain *Trichinellæ* which may cause disease, and since the absence of these worms cannot be guaranteed by any practical inspection now known, is unfit for food and therefore cannot be guaranteed if eaten raw. As Stiles has pointed out, great and unjustifiable loss may result from too stringent enforcement of the laws mentioned above.

CHAPTER XVI

THE HOOKWORMS AND THEIR ALLIES

(SUBORDER STRONGYLATA)

There is no group of the nematodes which cause more injury to man and more economic loss through attacks on his domestic animals, than the members of the suborder Strongylata. Although a few of these worms attack birds and lower vertebrates, the great majority are parasites of mammals. Many of them are peculiarly injurious due to the secretion of toxic substances which, when absorbed by the host, cause anemia, loss of vitality and general unthriftiness.

The worms of this suborder have one easily recognizable character which is constant and peculiar to them, namely a bursa surrounding the cloaca of the male. This is a sort of an umbrella-like expansion of the cuticle at the end of the body which is supported by fleshy rays comparable with the ribs of an umbrella. The arrangement of the rays is remarkably constant, and each ray is given a name. Usually the bursa consists of three lobes, two lateral and one dorsal, and it may or may not be split ventrally; in some species it is small, in others very large. The dorsal lobe is supported by a "dorsal" ray which may be bifurcated only at its tip or may be split almost to the base. From its root there arise a pair of "externo-dorsal" rays which usually enter the lateral lobes. The latter are supported by three pairs of lateral rays, arising from a common root, and two pairs of ventral rays arising from another common root. The names and arrangement of these rays as

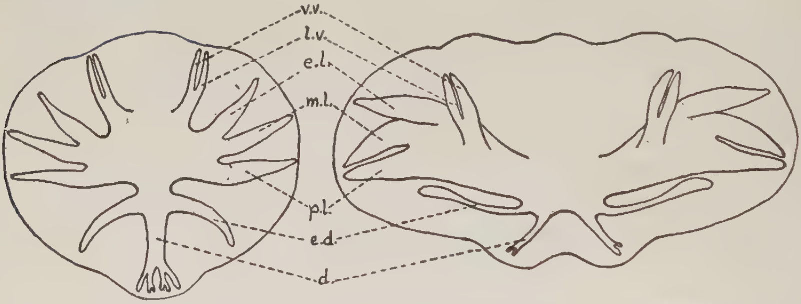

FIG. 131. Diagrams of bursas (spread out flat) of *Ancylostoma duodenale* (left) and *Necator americanus* (right), showing arrangement of rays; *d*, dorsal ray; *e.d.*, externo-dorsal; *e.l.*, externo-lateral; *l.v.*, latero-ventral; *m.l.*, medio-lateral: *p.l.*, postero-lateral; *v.v.*, ventro-ventral. (After Chandler, "Hookworm Disease.")

they occur in hookworms is shown in Fig. 131. Other characteristics of the group are the club-shaped muscular esophagus and the absence of distinct lips; the mouth is either a simple opening at the end of a fine slender head, or is provided with a more or less highly specialized buccal capsule. The eggs always have thin transparent shells which do not become bile-stained and are therefore colorless. They are in some stage of segmentation or contain embryos when laid. The eggs hatch outside the body into free-living larvæ which, after reaching a certain stage of development, enter a new host either by burrowing through the skin or by being ingested with water or vegetation.

The suborder is divided into three superfamilies, the Strongyloidea, including intestinal forms with a buccal capsule; the Trichostrongyloidea, including intestinal forms without a capsule but with a well developed bursa, and the Metastrongyloidea, including forms inhabiting mainly the respiratory or circulatory system, and having a small bursa with stunted rays. There are a number of families of Strongyloidea, of which three have representatives in man, — the Ancylostomidæ or hookworms, the Strongylidæ or strongyles, and the Syngamidæ or gape-worms. The other superfamilies contain only the single families Trichostrongylidæ and Metastrongylidæ, respectively.

Hookworms

There is no human worm infection which has attracted so much attention and has been the subject of so much investigation as hookworm. This is justifiably true, for there is no other worm infection which is as significant to the human race as a whole. Lane says that " as a world producer of death (often indirectly), of incapacity, and of misery, it is second to none, unless it be to malaria." Hookworm is never spectacular like some other diseases, it is essentially insidious; year after year, generation after generation, it saps the vitality and undermines the health and efficiency of whole races of people. In the course of a few summers a healthy family may become pale and puny; once industrious, they become languid and backward in work; once prosperous, they fall into debt; once proud, property-owning people, they are reduced to tenancy and poverty; the children, once bright and intelligent, become dull and indifferent, and soon fall hopelessly behind in school and drop out. The cumulative effects of this process on a race — physical, economic, intellectual and moral — handed down generation after generation, goes far toward explaining their backwardness. For years the " poor white trash " of some rural parts of our South were considered as a shiftless, good-for-nothing, irresponsible people, worthy only of scorn and of the sordid poverty and ignorance which they brought upon themselves as the fruits of their innate shiftlessness, but with the discovery that these unfortunate people were the victims of hookworms which stunted them physically and mentally, they became objects of pity rather than scorn, and through the unrelaxing efforts of the International Health Board of the Rockefeller Foundation, their unhappy lot has been greatly improved in the last fifteen years.

The history of our knowledge of hookworm is an interesting one. The first human hookworms were discovered in Italy, by Dubini, in 1838. In subsequent years they were discovered in Egypt, Brazil and other countries, and were suspected of causing the anemia which was so prevalent in those countries, but it was not until they were discovered, by Perroncito and others, to be the cause of an epidemic of severe anemia among laborers constructing the St. Gotthard tunnel in the Alps, that they were very seriously considered. It was not until 1901 that evidence was obtained of their wide distribution in southern United States.

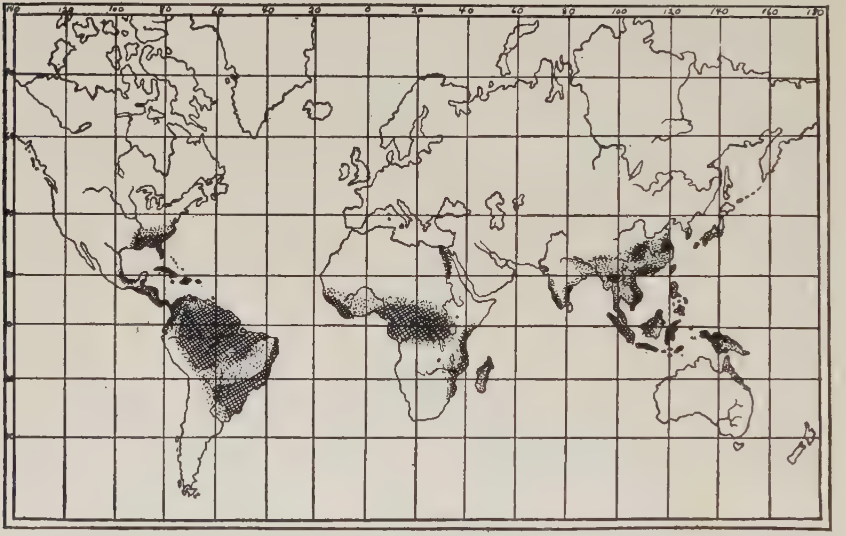

FIG. 132. Map showing distribution of hookworm infections. Crossed lines represent areas with heavy or moderately heavy infections. Stipple represents areas of light infections in a high percentage of individuals.

The general distribution of hookworm infection is shown in Fig. 132, the crossed lines representing areas where it is known or thought to be an important public health problem, and the dotted areas representing places where hookworm is common but is of less importance because the infections are for the most part light. Localities which have particularly severe infections in at least some large element of the population include the Gulf Coast States of America, some of the West Indies (especially Porto Rico), Central America, and the Amazon Valley and southeast coast of Brazil in the New World, and Egypt, West and Central Africa, a few localities in southeastern Asia and China, and some of the East Indies in the Old World. Hookworm also occurs outside of the warm, moist parts of the world in mines, where suitable conditions exist even as far north as England and Holland.

There are two species of hookworms which are common human parasites, *Ancylostoma duodenale* and *Necator americanus.* They both belong to the family Ancylostomidæ, but are placed in separate subfamilies. They are very similar in general appearance, and in most details of their life cycle, habits, etc., but *Ancylostoma duodenale* is much more injurious to its host, and is harder to expel by means of anthelmintics. All hookworms, including many species found in dogs, cats, herbivores and other animals, are rather stocky worms, usually about half an inch in length, with a well developed bursa, very long needle-like spicules, and with a conspicuous goblet- or cup-shaped buccal capsule, guarded ventrally by a pair of chitinous plates which either bear teeth, as in the ancylostomes, or have a blade-like edge, as in the necators and their allies (Fig. 133). The human ancylostome, *A. duodenale*, has two well developed teeth on each plate, with a rudimentary third one in front; *A. caninum*, common in dogs and cats, has three pairs of teeth, and *A. braziliense*, also common in cats and dogs, especially in the tropics, has one large tooth and a rudimentary one on each side. The latter species is an occasional human parasite, and its larvæ are a frequent cause of "creeping eruption."

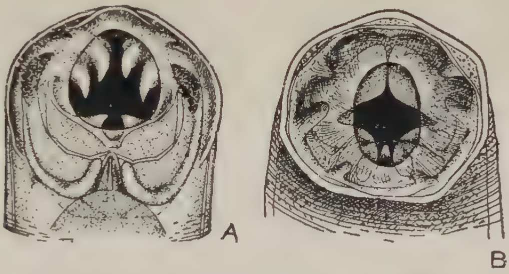

FIG. 133. Buccal cavity and mouth of Old World hookworm (*A*), and American hookworm (*B*), showing teeth in former and cutting ridges in latter. *A*, × 100; *B*, × 230. (After Looss.)

A. duodenale (Fig. 135) is primarily a northern species and predominates only in Europe, North Africa, western Asia and northern China, but it has accompanied infected mankind to all parts of the world; it is possible that it may have been the original species in at least a part of the American aborigines. It is larger and coarser than necator, the females averaging about 12 mm. and the males about 9 mm. in length. Freshly expelled specimens have a dirty rust color. The vulva of the female is behind the middle of the body and the tail is tipped by a minute spine. The males are easily recognizable by their broad bursas, which have the rays arranged as shown in Fig. 134*A*. The single dorsal ray and the nearly equal spread of the three lateral rays are good marks for distinguishing this species from necator, but after a little experience the two species, of either sex, can be separated with the naked eye by the form of the head, which in ancylostomes is coarse and only slightly bent dorsally, while in necators it is much finer and sharply bent. The structure of the mouth capsule of this species is shown in Fig. 133. *A. duodenale* is primarily a human parasite, but on rare occasions has been found in pigs, and experimentally can be occasionally reared in dogs, cats and monkeys. *A. braziliense* is a smaller and more slender worm, dead white or ivory colored, with a strikingly clear esophageal region in fresh worms. In some places in the tropics practically every cat and most dogs are infected with it, and in some localities, especially in Burma and some East Indian Islands, about 1% to 2% of the hookworms harbored by man are of this species. Particular interest attaches to it, however, from the fact that White and Dove (1928) showed that " creeping eruption " is caused by the penetration of the skin by the larvæ, and their subsequent creeping about just under the surface, apparently a reaction due to their presence in an abnormal host. Fulleborn (1927) found that a similar effect is produced by the European dog hookworm, *Uncinaria stenocephala*, which is more nearly related to necator.

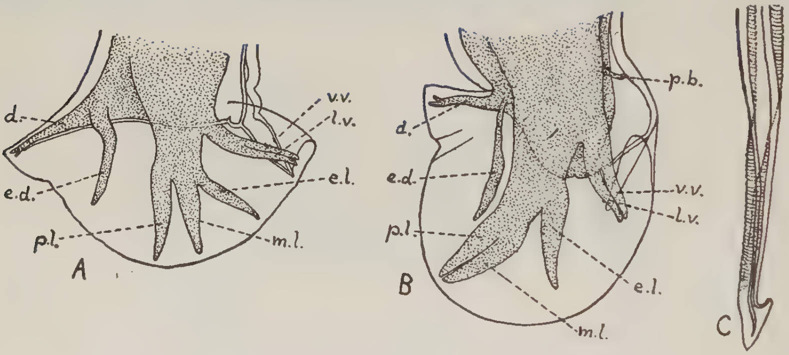

FIG. 134. Side view of bursas of *Ancylostoma duodenale* (*A*) and *Necator americanus* (*B*), and terminal portion of spicules of *Necator* (*C*). Abbreviations as in Fig. 131. (After Looss, from Chandler, "Hookworm Disease.")

Necator americanus is primarily a tropical worm, and is now the predominant species in all parts of the world except those mentioned in the last paragraph. It is often called the "American" hookworm because first discovered here, but is more likely African in origin. Thence it may have spread to India and to the Far East and Australia, and also to America; interesting evidence of past and present migrations of mankind can be traced in the hookworm fauna of various countries. Necator is smaller and more slender than *A. duodenale;* the females average 10 to 11 mm. in length and the males 7 to 8 mm. The vulva of the female is in front of the middle of the body, and there is no caudal spine. The bursa is longer and narrower than in the ancylostomes (Fig. 134*B*), and is distinguished by the split dorsal ray and approximation of two of the lateral rays. The structure of the mouth capsule is shown in Fig. 133*B*. *Necator americanus* is also primarily a human parasite, though capable of development in apes and monkeys, but a very similar form has been found in pigs in tropical America. Although regarded by

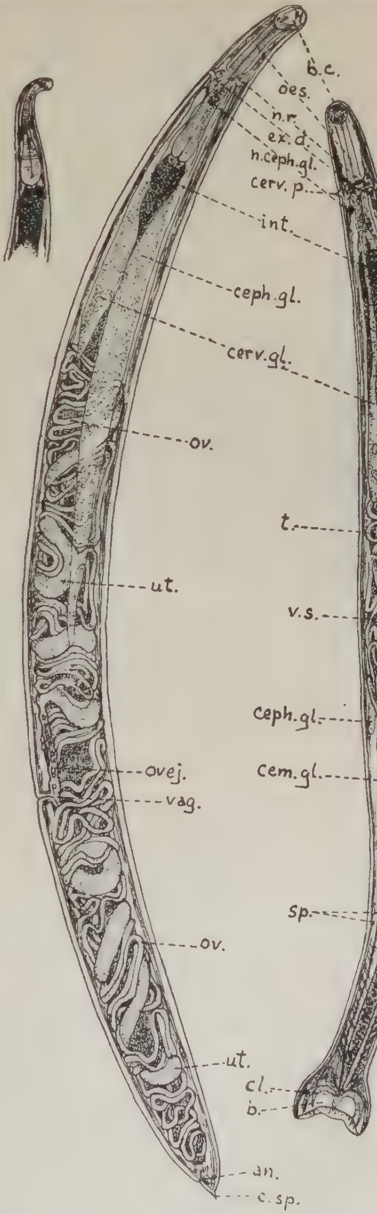

FIG. 135. *Ancylostoma duodenale*, female and male, with head of *Necator americanus* drawn to same scale; *an.*, anus; *b.*, bursa; *b.c.*, buccal capsule; *cem. gl.*, cement gland; *ceph. gl.*, cephalic gland; *cerv. gl.*, cervical gland; *cerv. p.*, cervical papilla; *cl.*, cloaca; *c. sp.*, caudal spine; *ex.d.*, so-called excretory duct; *int.*, intestine; *n. ceph. gl.*, nucleus of cephalic gland; *n.r.*, nerve ring; *oes.*, esophagus; *ov.*, ovary; *ovej.*, ovejector; *sp.*, spicules; *t.*, testes; *ut.*, uterus; *vag.*, vagina; *v.s.*, vesicula seminalis. (After Looss from Chandler, "Hookworm Disease.")

its discoverers, Ackert and Payne, as a separate species, *N. suillus*, it is thought by others to be the human species, slightly modified by its development in a strange host. Other species of necator have been described from chimpanzees.

The adult hookworms of both genera reside in the small intestine, where they draw a bit of the mucous membrane into their buccal capsules, and nourish themselves on blood and tissue juices which they suck (Fig. 136). Their main business in life is the production of eggs, and they tend strictly to business! Careful estimates show that each female necator produces from 5000 to 10,000 eggs per day, and ancylostomes over twice that many. Yet the bodies of the worms contain on the average only about 5% of this number of eggs at any one time. The eggs, which average about 70 by 38 μ in necators and 60 by 38 μ in ancylostomes, are in the four-celled stage of segmentation when passed out of the body with the feces, and do not develop further until exposed to air. They require moisture and warmth also, and if these conditions are present, and there are no injurious substances present in the feces, development proceeds so rapidly that an embryo hatches in less than 24 hours. Usually feces in the tropics are not left undisturbed, but are stirred up, aerated, and mixed with soil by dung beetles and other insects, which greatly improves the environment for the eggs and larvæ of hookworms. The embryos feed on bacteria and perhaps other matters in the feces, and grow rapidly. At the end of about two days they moult, then grow some more, and at the end of about five days they moult again. This time, however, the shed cuticle is retained as a protecting sheath, which may remain until the larva penetrates the skin of a host, or may be torn or worn away by the movements in the soil. The larva has now reached the infective stage. It eats no more, but subsists on food material stored up as granules during its five days of feasting. The optimum temperature for development is between 70° and 85° F.; lower temperatures retard and finally stop it, and in frosty weather the eggs and young larvæ are destroyed; higher temperatures decrease hatching and increase larval mortality. The infective larvæ of hookworms are about 500 to 600 μ in length, with characteristic form, color and movements which make them recognizable after some experience.

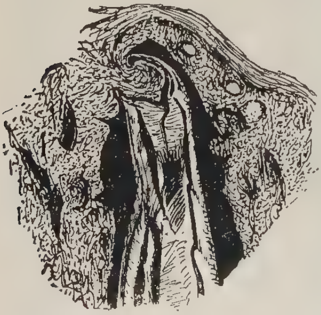

Fig. 136. American hookworm; section showing manner of attachment to intestinal wall. (After Ashford and Igaravidez, from photo by Dr. W. M. Gray.)

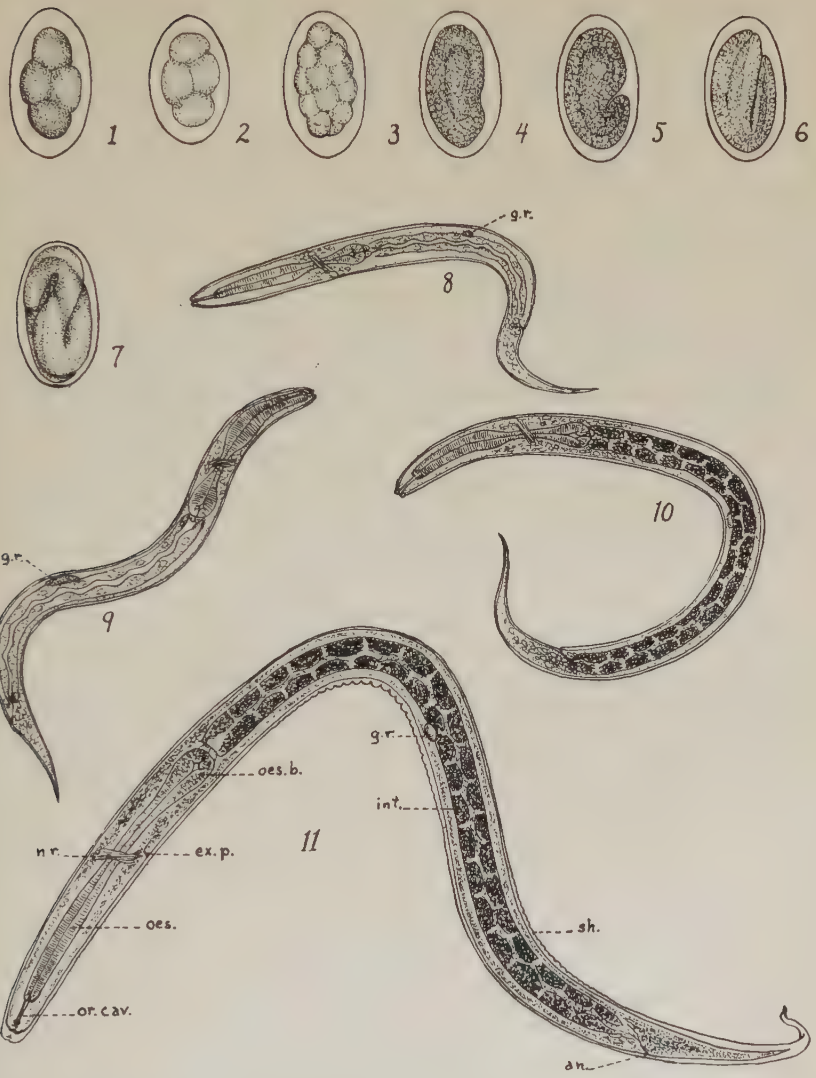

FIG. 137. Stages in life cycle of hookworms from egg to infective larva. *1*, egg of *Necator americanus* at time of leaving body of host; *2*, same of *Ancylostoma duodenale; 3* to *7*, stages in segmentation and development of embryo in the egg; *8*, newly hatched embryo; *9*, same of *Strongyloides* for comparison (note differences in length of oral cavity and size of genital rudiment, *g.r.; 10*, second stage larva; *11*, fully developed larva; *an.*, anus; *ex. p.*, excretory pore; *g.r.*, genital rudiment; *int.*, intestine; *n.r.*, nerve ring; *oes.*, esophagus; *oes. b.*, esophageal bulb; *or. cav.*, oral cavity; *sh.*, sheath. × 285. (After Looss from Chandler, "Hookworm Disease.")

There are also minute details of anatomy which make it possible to distinguish necator from ancylostome larvæ.

Much accurate knowledge of the biology of hookworm larvæ has been gained in recent years, largely due to the discovery of a method of extracting the larvæ from soil by Baermann (1917) and its improvement by Cort and his colleagues (1922). The most important contributions have been made by Cort, Payne, Riley, Augustine, Ackert and Stoll in the West Indies (1921–1925), by the writer in India (1924–1928), and by Svensson (1926) in China. The larvæ normally live in the upper half inch of soil, and commonly climb up to the highest points to which a film of moisture extends on soil particles, dead vegetation, etc. and extend their bodies into the air to await an opportunity to apply themselves to a human foot which is unfortunate enough to come in contact with them. When exposed to a hot sun or to superficial drying of the soil they retreat into crevices in the upper layer. Contrary to earlier opinion they do not migrate laterally but remain on the polluted spot, except to the comparatively slight extent to which they are distributed by rain, insects and other passive means. They do, however, migrate vertically when buried in loose-textured soil, even to the extent of two or three feet, in an effort to each a high point from which they can aerially extend themselves. In trenches or pits, however, they do not climb the walls, since, from the standpoint of the larvæ, the soil walls are very rugged paths, and before they have climbed more than a few inches they reach the top of some projecting particle, with no other particle directly above them which they can reach. From here they extend themselves, quite unaware that they have not reached a vantage point at the top, and are thus trapped. The larvæ are strongly attracted by heat, and are stimulated to activity by contact with objects, and it is these reactions which cause the larvæ to burrow into the skin of animals.

Since the larvæ have only the stored food granules on which to subsist until a suitable host is reached, the more active they are the sooner their food supply is used up and the sooner they die. Vertical migration through even a few inches of soil is a very expensive process for them. Under tropical conditions, where alternations of sun and shade and of heat and coolness, and also disturbance by rain, insects, etc., stimulate them to frequent movement, their span of life is not nearly so long as it was thought to be; about 90% of the larvæ have succumbed in two or three weeks, and almost all are dead in six weeks. On the other hand, larvæ kept in water in a cool place, and left undisturbed, may live for 18 months or more. Larvæ which have had their reserve food greatly depleted, although still alive, may not have enough energy to penetrate the skin of a host.

Infection normally takes place by penetration of the skin by the larvæ; this important discovery was first made by Looss (1898) when he accidentally spilled some water containing larvæ on his hands, and acquired an infection. The larvæ burrow until they enter a lymph or blood-vessel and are then carried by the blood stream to the right heart and thence to the lungs, where they are usually caught in the capillaries and again proceed to burrow, this time into the air spaces of the lung. The ciliary movement of the epithelium of the bronchial tubes and trachea carries them to the throat, whence they are either expectorated with sputum, or swallowed. In the latter case they go to the intestine and bury themselves between the villi and in the depths of glands for a brief period until the third moult is completed, after which they are provided with a provisional mouth capsule and can successfully adhere to the mucosa. It is possible for the larvæ to cause infection when swallowed with food or water also, though in nature this must be of relatively rare occurrence. The fate of swallowed larvæ and the course of their migrations in the body have been investigated particularly by Fulleborn (1914–1927), Yokogawa (1926), and Scott (1928). Some of the larvæ bore through the mucous membranes and go through the roundabout path through the body, especially in abnormal hosts, but in normal hosts the majority of swallowed larvæ bury themselves in glands for a few days and then establish themselves in the intestine directly. The third moult may occur as early as three days after infection, but may be delayed for several days longer. The larvæ grow rapidly to a length of from 3 to 5 mm. and then moult for the fourth and last time, with the acquisition of the definitive mouth capsule, and the development of reproductive organs. In man it is usually about six weeks after infection that eggs first begin to appear in the feces.

The length of life of the adult worms in the intestine may be five years or more, but is much shorter in the case of the majority of the worms. According to my own investigations, there is evidence that in the absence of re-infection about 50% of the worms acquired during a favorable season are lost within three or four months, 60% in six months, 70% in a year, and 80% in two years. This, if confirmed, means that under ordinary conditions infections are rapidly acquired and rapidly lost, and that in countries which have wet and dry seasons little cumulative increase in worms can occur on account of the large annual reduction in worms during the dry season when re-infection is stopped.

Epidemiology. — Much valuable epidemiological information has been obtained in recent years by the work of Baermann in Sumatra, Darling in Malaya, Smillie in Brazil and Alabama, Cort and his colleagues in the West Indies, China and Panama, and the writer in India. There are many factors which influence the amount of hookworm infection in a community. Temperature, as already intimated, is a prime controlling factor. Rainfall is also of fundamental importance. The data available indicates that heavy hookworm infections are never common in localities having less than 40 inches of rain a year, and that with larger annual rainfalls much depends on the seasonal distribution and on the distribution within each month, for hookworm larvæ will not withstand desiccation, and a drying of the soil to a depth of even an inch practically sterilizes it. Such local facts as humidity, drainage and hygroscopic nature of the soil also influence the effectiveness of short rainless periods. The nature of the soil is very influential; hookworm never thrives in regions of heavy clay soil, whereas in adjoining areas with sandy or humus soil it may constitute an important problem. Salt impregnation of soil is also injurious. Vegetation exerts an influence, since dense shade is far more favorable for the development and longevity of larvæ than is light shade or exposure to sun. Irrigation may make rainless regions favorable for hookworm if, as in Egypt, moistened soil is selected for defecation, but in extensively irrigated areas in western India there is practically no hookworm because dry spots are always available for defecation and are preferred. Animals which devour feces, especially in the tropics, such as pigs, dogs, cattle, etc., exert an influence, since in pigs and dogs the eggs in fresh feces pass through the animals uninjured and may be voided with the feces of the animals in places where they are more, or less, likely to cause infection. In chickens, and probably in cattle also, on the other hand, most of the eggs are destroyed when ingested. Insects play an important rôle. Dung beetles are allies of hookworms since they mix feces with soil and render the cultural conditions far more favorable; cockroaches, on the other hand, destroy most of the eggs in their " gizzards," and were found by the writer to play an important part in keeping down hookworm infections in Indian mines.

Many human factors also affect the amount of hookworm. Some races are more susceptible than others. The white race is particularly susceptible and negroes very slightly so. The other races would appear to occupy a more or less intermediate condition. Age and sex influence the amount of infection due to differences in habits, and also affect the injury done by a given number of worms, for females are more injured than males and children more than adults. Occupation is often a determining factor, in so far as it leads to habits which render the acquisition of worms more likely. In most countries agriculture and mining are the main hookworm occupations, but in most places the infection is not strictly agricultural but merely rural. The raising of such crops as coffee, tea, sugar, cacao, and bananas is particularly conducive to hookworm in soil-pollution countries, since they are grown in moist, warm climates under conditions affording an abundance of shade and suitable soil; cotton and grain raising is much less dangerous since these crops are grown in drier areas, and cotton in unfavorable soil. Raising of rice and jute, mainly on flooded ground, is not associated with heavy hookworm infections. In China and Japan, where night-soil is used as fertilizer, hookworm infection is more strictly agricultural, and varies greatly with the type of crop produced and the manner in which the night-soil is used. Especially heavy infections occur in mulberry-raising districts, since ideal conditions for hookworm propagation are afforded.

Defecation habits are also of great importance. In soil-pollution countries the greater part of the infections are acquired while standing on previously polluted ground during the act of defecation. The concentration of the defecation areas, the extent to which people mingle in common areas around villages, the type of places selected, etc., are all influential factors. Wherever simple soil pollution is modified by the use of standing places or primitive latrines which keep the feet off of the polluted ground, and bring about an unfavorable concentration of fecal material, hookworm infections are light. Shoe-wearing also affords a high degree of protection; in southern United States and Queensland hookworm infection is almost entirely limited to children under fourteen to sixteen years of age, since after the age of fourteen shoes are habitually worn. Even simple sandals or wooden soles without uppers, as worn in parts of India, are effective. Expectoration habits also have an important effect; those individuals who habitually spit out phlegm which collects in the mouth get rid of many of the hookworms which invade the body, but others allow them to grow to maturity. It has become a prevalent notion in our Southern States that tobacco-chewing is conducive to health, and that habitual chewers are seldom severely victimized by hookworms. This is not due to any virtue in tobacco juice, but to the fact that the constant spitting in which these people indulge greatly increases the hazards of hookworm larvæ which are endeavoring to reach the intestine. Diet may have some influence on the welfare of hookworms in the intestine, and it undoubtedly influences the development of the eggs in the feces, but its most marked bearing is on the effects produced by the worms; undernourished individuals may suffer severely from relatively light infections, whereas well-nourished and otherwise healthy persons may harbor many hundreds of worms without evident ill effects.

Pathology. — The first injury done by hookworms is the production of " ground itch " or " water sore " where they enter the skin; this consists of little blister-like vesicles which often develop into pustular sores due to bacterial invasion. Some " foreign " species of hookworms, such as *Ancylostoma braziliense* and *Uncinaria stenocephala*, remain in the skin and form tortuous eruptions as they wander about, causing the condition known as " creeping eruption " (Fig. 138). The next effect is in the lungs, where the larvæ may open up portals of entry for bacteria of pneumonia and influenza or, if numerous, even cause pneumonia symptoms themselves. A few weeks later, after establishment in the intestine, they cause abdominal discomfort and more or less interference with the normal functioning of the digestive system. With the absorption of toxic substances, produced by the worms, and perhaps also of bacterial or food toxins absorbed through the intestinal lesions, the blood-forming organs are affected, and the patient may become anemic, with reduced number of corpuscles, still more reduced hemoglobin, and more or less eosinophilia. In hookworm countries where worms are constantly being picked up no such stages in the disease are recognizable, but different degrees of severity of the infection can be observed, dependent, among other factors, on the number of worms harbored.

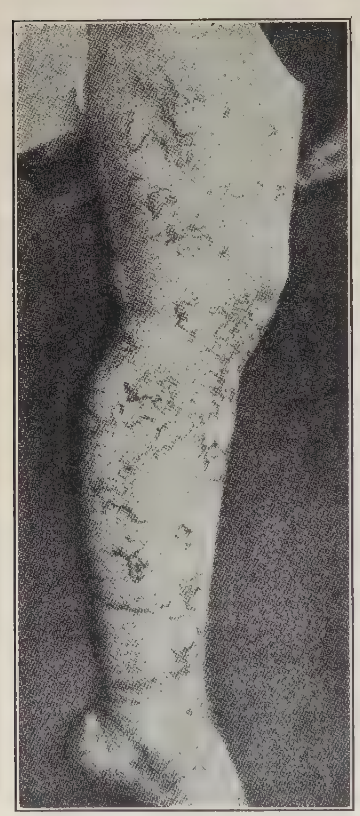

FIG. 138. A case of " creeping eruption," about two weeks after infection. (After Kirby-Smith, Dove and White.)

Even in localities where heavy infections are prevalent, many infected individuals show no symptoms whatever, and one must distinguish between hookworm infection and hookworm disease. This is due to the fact that in well-nourished and otherwise healthy individuals the injury to the blood can be compensated as rapidly as it is produced. This, of course, draws on reserve vitality and may reasonably be supposed to reduce resistance to disease or fatigue, and in children the energy required to keep the hemoglobin up to standard interferes with normal growth, thus causing a stunting in size. It is only when the repair cannot keep pace with the damage that obvious symptoms appear. These are largely the result of anemia and proportional to it. In severe cases the hemoglobin may be reduced to 30% or less, with 2,000,000 or less corpuscles per c.mm. The most noticeable symptoms are a pallor proportionate to the anemia; a very marked languor and indisposition to play or work, popularly interpreted as laziness; a flabbiness and tenderness of the muscles; breathlessness after slight exertion; enlargement and palpitation of the heart, with weak and irregular pulse; edema, which gives a puffy appearance to the face and contributes to a "pot-bellied" condition of the abdomen; a dull fish-like stare in the eyes; reduced perspiration; more or less irregular fever; and heart burn, flatulence and abdominal discomfort. The appetite is capricious, and frequently there is an abnormal craving for coarse "scratchy" subtances such as soil, chalk, wood, etc. Severe hookworm cases in our Southern States are very often "dirt-eaters," though they will rarely admit it. Retardation in both physical and mental development is a natural result of anemia in children; not infrequently a girl or boy of 14 or 15 years of age, heavily infected since early childhood, will have the development of a child of 9 or 10, and puberty may be long delayed. As would be expected, there is a lowered resistance to fatigue, to malnutrition, to other diseases, and to any other devitalizing influences. The mental retardation results in stupidity and backwardness in school, and there are sometimes other nervous manifestations, such as dizziness, insomnia, optical delusions, general nervousness, and fidgety movements.

The loss of efficiency from hookworm infection is often startling, and on plantations, tropical estates, mills, mines, etc., may be the cause of a loss in efficiency on the part of the laborers amounting to 25% or even 50%, involving great economic loss from inefficient labor, sickness and hospitalization, death, lowered birth rate, etc. When the inhabitants of whole countries have their life-giving blood reduced to 50% of its normal efficiency, it is easy to understand their low mental and physical condition. Unlike many diseases, hookworm has no tendency to weed out the weak and unfit; it works subtly, progressively, undermining the health and welfare of the community, each generation handing down an increased handicap to the next until an equilibrium is reached in which poverty, ignorance, and physical unfitness are the outstanding characteristics.

There has been much discussion about the injuriousness of light hookworm infections. In earlier days all infected individuals were lumped together in contrast to those in whom infection was not demonstrated by methods of examination then in vogue. The amount of hookworm in a locality was judged by the percentage infected, and much evidence was obtained which demonstrated the greater healthiness and efficiency of the uninfected group. Darling, in 1918, was the first to emphasize the importance of the number of hookworms harbored. In the Orient, and later with Smillie in Brazil, he substituted average number of worms harbored for percentage infected in estimating the importance of hookworm in a community, but the difficulty involved in determining the average worms harbored, which had to be done by counting worms passed after anthelmintic treatment of a relatively small sample of the population who could be kept confined or trusted to keep all stools passed, made progress slow. In 1923 Stoll devised an easy method of counting the eggs per gram in the feces of infected people, and demonstrated that there was a rough correlation between eggs per gram and number of worms harbored. The substitution of Stoll's egg-count method for worm counts, and its wide application in hookworm surveys, has revolutionized our knowledge of hookworm infection since that time, and has done more than any other thing to accelerate scientific hookworm control. It has revolutionized administrative procedures; it has given an index to the necessity for control measures and the kind of measures called for; it has given a measure of improvement after sanitary reforms, and of the efficacy of anthelmintics; and it has provided a basis for the scientific study of the effects of different degrees of infection under varying conditions. By this means it has been demonstrated that light infections with 50 worms or less, and under some conditions with many more, are practically harmless and can ordinarily be safely ignored. Moderately heavy infections may produce no measurable symptoms under otherwise perfect conditions, but make themselves felt when the diet is inadequate, when the individual is exposed to hardships

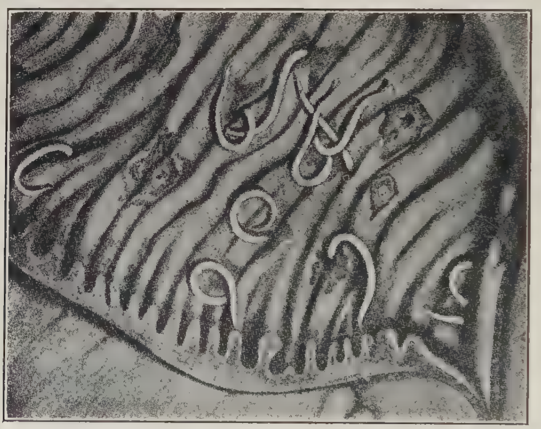

FIG. 139. Hookworms on wall of intestine, showing lesions. After International Health Board.

or overwork, or when he is suffering from other chronic diseases. Heavy infections with over 500 worms usually produce obvious symptoms. It is not feasible to set any definite limits to these grades of infections so far as individuals are concerned, for one person may be apparently unaffected by 500 worms when another will suffer from 100, but averages in particular communities give valuable information as to the injuriousness of different grades of infection under the existing conditions of race, age and sex, diet, hygienic conditions, etc., and extremely valuable information concerning the influence of epidemiological factors can be obtained. The erroneousness of judging hookworm infection by the percentage of people infected is nowhere better demonstrated than in Bengal. In that country, with its 46,000,000 inhabitants, an average of at least 80% of the people are infected — a condition which a few years ago was spoken of as " staggering." But egg counts show that in 90% of the area of Bengal the average worms harbored per person is less than 20, and not more than 1% of the people have over an estimated 160 worms and none over 400. In other words, instead of being a staggering problem involving the health of over 35,000,000 people, it is negligible from the public health point of view.

Diagnosis. — Hookworm infection can rarely be diagnosed by symptoms, but a positive diagnosis is easily obtainable by modern floatation methods of finding eggs in the stools. If it is only desired to find infections which need treatment the simple smear method suffices, but more accurate diagnosis can be made by the Willis method or Lane's D. C. F. method (see p. 211). Quantitative diagnosis, the importance of which has been indicated, can be made by the egg count methods of Stoll (1923) or of the Caldwells (1926). Community diagnosis, *i.e.*, the relative degree of severity of the disease in a community, can be indicated by ascertaining the weighted mean egg count as described by the writer (1929).

The collection of fecal samples for diagnosis on a large scale can be made either in tightly closed ½ ounce tin boxes, or better still in bottles containing a few cc. of antiformin as described by Maplestone (1929). In either case the specimens can be sent to a central laboratory for examination, thus eliminating the necessity for a moving field laboratory, for the specimens are useful both for diagnosis and egg counts even after several days.

Treatment. — The treatment of hookworm infection has undergone an interesting evolution, and more advance has been made towards the goal of an ideal anthelmintic for hookworms than for any other common helminthic infection. Until 1879 the powdered rhizomes of male fern, and subsequently the extract of male fern, which is still one of our best drugs for expelling tapeworms, was most commonly used for expelling hookworms also, but with very indifferent success. In 1880 Bozzolo introduced thymol for expelling hookworms, with much better success and, with beta-naphthol as an alternative, this was the classical drug for treatment of hookworm disease until a few years ago. Thymol is very poisonous but can be taken in relatively large doses by mouth because it is very slightly soluble in water, and is therefore not absorbed. It is freely soluble in alcohol and fats, however, and fatal results frequently occur when such substances are taken with thymol. A preliminary starvation period and purge, the necessity of remaining in bed during treatment, and frequent unpleasant and alarming symptoms such as fainting and collapse, are objectionable features of the thymol treatment when used on a large scale or in field work. A dose of 60 grains expels about 75% of necators and about 60% of ancylostomes. Beta-naphthol in 50 to 60 grain doses is slightly less effective, and it often has severe effects on the kidneys, and more frequently is dangerously toxic, especially in malaria infections.

During the European war, when thymol was unobtainable, oil of chenopodium, which had previously been tried, came into favor, and with improvement in its preparation and methods of administration it was soon demonstrated to be not only a substitute for thymol, but a distinctly superior drug, both for hookworm and ascaris. Being made from a common weed, the supply is inexhaustible. It is more effective than thymol, removing about 90% of necator and 75% of ancylostomes in one treatment with 30 minims, divided into three 10-minim doses in capsules at hourly intervals, and followed by a saline purge. No preliminary starvation or purge is required, and the patient need not remain in bed. The active principle, ascaridol, is sometimes extracted and used in place of the whole oil. The drug has a toxic effect on the nervous system but is less dangerous than thymol, and seldom produces alarming symptoms, although very young children and old and weak people do not tolerate it well.

In 1921 M. C. Hall demonstrated that carbon tetrachloride was almost 100% efficient for removing hookworms in dogs, and subsequent trials showed that it was more efficient for human beings than any drug previously used, could be administered in one dose without preliminary starvation, ordinarily caused no symptoms other than slight giddiness and somnolence, and in a dose of 3 to 4 cc. was practically harmless. Since then over a million cases have been treated with it. It is best given in salts or emulsified in milk and followed at once or later by a purge. Like thymol it is soluble in alcohol and fats.

The drug is highly toxic when it gets into the general circulation, but when absorbed from the intestine the liver tissue takes it up so that this general toxic effect is avoided, but when absorbed in large quantity it has a highly injurious effect on the liver itself. In the therapeutic dose, however, the damage to the liver is ordinarily negligible, and is quickly repaired, unless the liver is already damaged. Alcohol, a fat diet, and starvation all tend to increase the livery injury. Occasional fatal cases occur in patients in whom, as Minot has shown, calcium is deficient due to a diet inadequately supplied with this substance, and severe cases of carbon tetrachloride poisoning can usually be improved in a most striking manner by the administration of calcium. The condition of the patient as regards diet and health of the liver has much more to do with the toxicity than the size of the dose. Doses in excess of 12 cc. have been taken without injurious effects, whereas fatalities have been recorded with a dose of only 1 cc. One dose removes from 90 to 98% of necators and about 80% of ancylostomes. When ancylostomes and ascaris are present as well as necators, a combination of carbon tetrachloride and oil of chenopodium is more effective than either drug alone and no more toxic. The writer has used 3 cc. of carbon tetrachloride together with 10 to 15 minims of oil of chenopodium with excellent results.

Still more recently tetrachlorethylene has been introduced as a substitute for carbon tetrachloride, with very promising results; in contrast to carbon tetrachloride it is practically not absorbed at all in dogs, and is never toxic to them

In recent years mass treatment, first advocated by Darling, has come into extensive use, and has been the means of greatly speeding up hookworm campaigns. By mass treatment is meant the wholesale treatment of a community at one time, when the great majority of the individuals are found to be infected, without preliminary diagnosis. The diagnosis itself does not require so much time, but the difficulty in obtaining fecal samples from primitive people is well known to anyone who has tried it; in many cases it is quite impossible. If all the members of a community are treated at once, preferably in a dry or cold season when rapid reinfection from an already badly infested soil cannot occur, the reduction in infection is striking and durable. In Fiji practically the entire population was treated in two years, a feat which could not have been accomplished in any length of time by the older methods, since long before even a fair percentage of the people could have been covered by diagnostic measures, those first treated would again have been infected from their untreated neighbors. The original mass treatment in Fiji was made in 1922 and 1923, and in 1924 the more heavily infected areas were treated again. In 1928 Lambert reported that clinical hookworm disease was still rare in Fiji; the people are healthier, happier and more prosperous, and hookworm has been eliminated as an economic factor.

Prevention. — Theoretically there are few if any diseases which can be as simply, as certainly, and as easily controlled as hookworm. Diagnosis is easy and accurate, treatment reduces existing infections to a negligible point, and reinfection can be prevented by stopping soil pollution, for no other animals, except possibly pigs and apes, and these only in some localities, harbor human hookworms. But in the prevention of soil pollution the sanitarian runs into a snag. The difficulties involved in this seemingly simple procedure are infinitely greater than the average inhabitant of a civilized sanitary country would suspect. It involves an attempt to induce hundreds of millions of people in tropical and subtropical countries to abandon habits which have been ingrained in them for countless generations, and in some instances dictated by religion, and adopt in their place unfamiliar habits which appeal to them as obnoxious and undesirable, and the reasons for which they cannot readily grasp. Even in our own Southern States there are unexpected difficulties; a survey in the early part of the present century showed that in the hookworm belt about 68% of the rural homes were unprovided with privies of any kind, and any traveler through the rural parts of these states at the present time, after more than 20 years of education and exhortation, will find the conditions little improved in many places. In many rural districts where privies do exist, their use is restricted to the women and children or to the family of the manager. Among the "jibaros" or plantation laborers of Porto Rico, of 61 hookworm patients who were questioned, 55 never had used privies of any kind, and of the six who did occasionally use them, only two lived in rural districts.

Only four weapons are available for use in the control of hookworm: — treatment, protection of the feet with adequate footgear, disinfection of feces or soil, and prevention of soil pollution. Mass treatment gives immediate relief, and slows up the rate of reinfection on account of the great reduction in number of eggs reaching the soil, but treatment alone, unless consistently repeated, is inadequate, since it has never yet, and probably never will be, found feasible to eliminate all the worms, and reinfection inevitably follows. In Porto Rico, Hill (1927) treated 1000 people in an isolated valley and eliminated 97.5% of the worms. In one year the residual infection increased to 500% and was nearly 20% of the infection before treatment.

Wearing of footgear is a valuable measure when it can be consistently enforced, and is essential for individuals in infected areas who desire to protect themselves, but it is often as difficult to enforce in the tropics as is sanitary disposal of feces, and is far less effective in ultimate control.

It is a valuable temporary measure, comparable with the use of mosquito repellants for the control of malaria, but it does not get at the root of the trouble.

Disinfection of soil or feces is difficult. Salt can be effectively used under certain conditions, especially in mines, and lime added to feces is an effective method of killing hookworms in night-soil. In general, however, disinfection methods are not feasible.

Prevention of soil pollution, then, remains as the only dependable method of hookworm control under most conditions, but the time when the value accruing from proper sanitation will be realized to an extent sufficient to make man as careful concerning his personal habits as are some of his domestic animals is still far off; eventually it will be reached. It is significant that the domestic cat, which sanitarily covers up its excreta, has on the average far fewer intestinal parasites, of those species acquired from contamination of food or water, than has the less careful dog. It is a mistake of many sanitarians to try to accomplish too much all at once, and to force on the tropical native our own ideas of sanitary privies, just as we try to force on him our ideas of ethics, religion, clothing, and food habits. By building up from native practices already existing, such as, in many places, the use of standing places or primitive types of latrines, more could be accomplished than by erecting our own types of latrines, which quickly become smelly and filthy, and highly obnoxious, when used by people who have no training or experience in keeping them clean. In this, as in most other things, results can be obtained most effectively in the long run by beginning in a simple way, by patient education, and by consideration for the ideas and prejudices of the people to be dealt with. It is better as a beginning to teach the coolie to defecate into a trench, from a log over a ditch, or from a low branch or root of a tree or even from a projecting stone, than to build an enclosed fly-proof latrine, which he promptly befouls, and which prejudices him against latrines in general. Meanwhile education with respect to the mode of infection of hookworm, brought home by demonstrations of the nematodes in soil, with appeals to local prejudices and superstitions, may help greatly, and eventually really sanitary privies, to control such diseases as dysentery and typhoid as well as hookworm, will be possible.

The campaign against hookworm disease, which has been sponsored especially by the International Health Board, although a most worthy end in itself, leads to even greater benefits, for the work, while bringing relief to hundreds of thousands of suffering people, is at the same time serving the more useful purpose of creating a popular sentiment in support of permanent agencies for the promotion of public health. In the United States it has led to rapid advances in rural hygiene and the establishment of county health organizations all over the country, and similar local organizations have been brought to life in many other countries. In Brazil, entirely as an outcome of a hookworm campaign, appropriations for rural sanitation grew from nothing in 1916 to over $2,000,000 in 1922. Schools of Hygiene have been established in various parts of the world to provide trained men to carry on the work. The ultimate results which may come from the simple beginnings centered on the eradication of hookworm disease are impossible to estimate, but in the light of the tremendous accomplishments which we have seen realized since the inception of the work of the International Health Board less than 20 years ago, the outlook for the future is bright indeed.

Other Strongylata

As already mentioned, species of *Ancylostoma* are important parasites of dogs and cats; dogs in Europe commonly suffer from infection with *Uncinaria stenocephala;* and sheep, goats, cattle, etc., from species of *Bunostomum*, both of which belong to the same subfamily as *Necator*.

Family Strongylidæ. — The members of this family have a well-developed buccal capsule which lacks ventral teeth or cutting plates but has a "corona radiata" or crown of leaf-like processes guarding its entrance (see Fig. 140); it contains a number of species which are injurious to domestic animals, and a few which are more or less frequent parasites of man. Among the more important forms are species of *Strongylus* and *Trichonema* in horses, *Chabertia* in sheep and goats, and *Œsophagostomum* in pigs and ruminants.

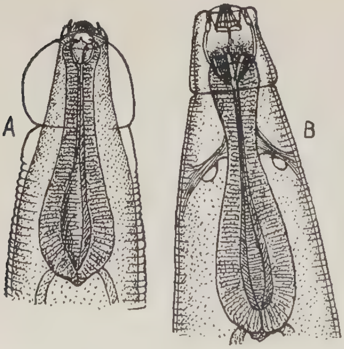

Fig. 140. Heads of *Œsophagostomum brumpti* (*A*) and *Ternidens deminutus* (*B*). (After Railliet and Henry, from Brumpt.)

The esophagostomes or nodular worms, aside from being common and injurious parasites of pigs, sheep, goats and cattle, are very common parasites of apes and monkeys, and occasional parasites of man. They rather resemble hookworms in general appearance, but are larger, and have different heads and bursas. The early life cycle is incompletely known, but is believed to be similar to that of hookworms. On reaching the intestine of the host, however, the worms do not at once establish themselves in the lumen, but burrow into the lining of the large intestine where the host forms a tumor-like capsule around them (Fig. 141). The large intestine of a badly infected animal may be covered with nodules about half an inch to an inch in diameter, filled with a thick, greenish, pus-like or cheesy substance, together with an immature worm. When approaching maturity the worms escape into the cavity of the large intestine, where the sex organs develop to maturity and the eggs, which closely resemble those of hookworms, are deposited.

Several species of these worms, normally inhabiting apes and monkeys, have been found on rare occasions in man, but since the eggs are indistinguishable from those of hookworms, and diagnosis of the encysted worms can be made only at autopsy, human cases may be much commoner than is suspected. There is a difference of opinion as to the species involved. A single human case in Brazil was due to a species called *O. stephanostomum* var. *thomasi*, while *O. brumpti* (Fig. 140*A*) has been recorded from man once in East Africa and once in New Guinea; by some this is considered identical with *O. apiostomum* found in man in Nigeria; 4% of the prisoners in a Nigerian jail were recorded by Johnson as being infected. Most of these cases were light, but the Brazilian case was severe, and probably the parasites were the cause of death. In ruminants and apes the infection commonly produces severe emaciation and prolonged dysentery and sometimes fatal peritonitis. In the encysted stage the worms are unaffected by anthelmintics, and are difficult to dislodge even when free on account of their location in the large intestine.

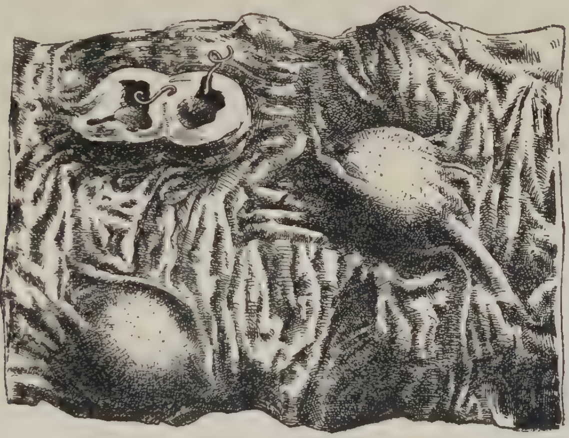

Fig. 141. Tumors or nodules of *O. brumpti* in the large intestine of an African. $\frac{3}{4}$ nat. size. (After Brumpt.)

A related worm, *Ternidens deminutus*, has been recorded several times in natives of central East Africa, usually having been confused with hookworms. Sandground (1929) has secured evidence that the worm may be fairly common in Southern Rhodesia. It is closely related to the esophagostomes, and probably like them lives in cysts in the large intestine when young. The slightly asymmetrical eggs are larger and more pointed at one end than are those of hookworms, and are in an advanced stage of segmentation when freshly passed. They develop into infective larvæ much like those of hookworms, which cause infection when experimentally swallowed. The worms superficially resemble hookworms, but differ in the buccal capsule. The latter, which is shallow in *Œsophagostomum,* is deep and goblet-shaped, with three teeth in its depths, in *Ternidens* (Fig. 140).

Family Syngamidæ. — This family includes worms which live in the trachea and bronchi of birds and mammals, and are commonly called gape-worms or forked-worms. They have a relatively huge cup-like buccal capsule which has no teeth or cutting plates on its ventral edge, nor any corona radiata, but is reinforced by a prominent chitinous ring, and has some small teeth in its depths. The males and females always occur in pairs, the male permanently attached to the vulva of the female by its bursa, so that the pair have a forked appearance (Fig. 142); the females are usually about 15 to 20 mm. long. The eggs resemble those of hookworms except that they have a pair of minute polar caps and thicker shells. After being deposited in the air passages they are coughed up and swallowed, passing out in the feces. They then develop into infective larvæ after the manner of hookworms. When swallowed they penetrate the mucous membranes and are carried to the lungs by the blood stream. One species of *Syngamus* is an injurious parasite of turkeys and young chickens, and a related worm affects geese. One instance of human infection with a gape-worm was discovered in the West Indies, where a pair of worms was found in the sputum of an Irish woman. Leiper (1913) named the worms *S. kingi* after their discoverer. The normal host of the worm is unknown.

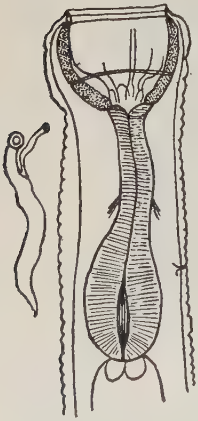

FIG. 142. Right, Head of female *Syngamus kingi* (after Leiper); left, a pair of worms in copula.

Family Trichostrongylidæ. — The members of this family, which are at once recognizable by the finely drawn out head without a buccal capsule, together with a well-developed bursa in the male (Fig. 143), are also very important parasites of domestic animals. Sheep and goats suffer severely from the stomach worm, *Hæmonchus contortus*, and to a less extent from species of *Trichostrongylus*, *Cooperia*, *Nematodirus* and *Ostertagia*. The latter genera also infest cattle. The life cycles of these worms, insofar as they are known, are essentially the same as that of the hookworms, but infection probably occurs more frequently by swallowing infective larvæ with vegetation than by penetration of the skin. They produce symptoms of anemia, emaciation and general unthriftiness, and many young animals die from heavy infections.

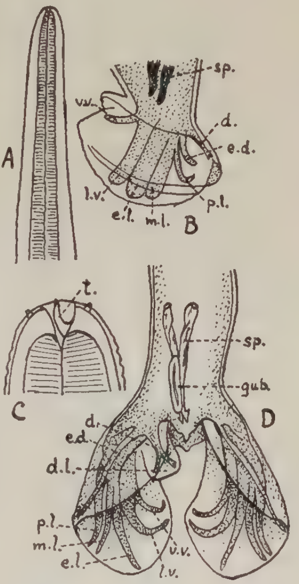

Fig. 143. *A* and *B*, head and bursa of *Trichostrongylus colubriformis;* *C* and *D*, head (greatly enlarged) and bursa of *Hæmonchus contortus;* *t.*, buccal tooth; *d.l.*, dorsal lobe, other abbreviations as in Fig. 131. (*A*, original; *B*, after Looss; *C*, after Yorke and Maplestone; *D*, after Ransom.)

Fortunately man is not subject to severe infections with these parasites. Several species of *Trichostrongylus* (*T. colubriformis*, *T. probolurus* and *T. vitrinus*), which are normally parasitic in the small intestine in sheep, goats and camels, occur as occasional human parasites, having been so recorded especially in Egypt, Armenia, and India. In China and Japan, especially in Korea, another species, *T. orientalis*, subsequently found also in Armenia, has been found fairly commonly in agricultural peasants, and has been found by Faust in sheep and camels in North China. Jimbo (1914) reported over 200 cases in Japan. The eggs of these worms are larger than those of hookworms, more pointed at one end, and in a later stage of segmentation when passed by the host, but are undoubtedly often passed over as hookworm eggs. In India the writer found cases all over the country, averaging about 1% in some provinces, and in some, particularly sheep- and goat-raising localities, notably in Kashmir villages, 14 to 18% of the people had light infections. The species cannot be distinguished by the eggs, and the worms, being very small and protected by mucus, are difficult to dislodge by treatment, and even if dislodged are hard to find in the feces; for these reasons it was not possible to identify the species of the Indian worms. The trichostrongyles are minute, reddish worms, 4 to 6 mm. in length and only about 80 μ in diameter, which is only about a fifth the diameter of a female necator. The spicules are short and stumpy, and the females have the vulva near the middle of the body. The uterus contains relatively few eggs, which are very large in proportion to the size of the worm. In severe infections they produce an anemia similar to that produced by hookworms. The stomach worm, *Hæmonchus contortus*, which often plays havoc with lambs and kids, and is an extremely common parasite of these animals all over the world, has been found once in man in Brazil, and Sweet found three probable cases, diagnosed by eggs, in Australian aborigines. The worm usually inhabits the fourth stomach of sheep and goats, and occasionally the duodenum. It is much larger than the species of *Trichostrongylus*, the females being 18 to 30 mm. and the males 10 to 20 mm. in length, with diameters of 400 and 500 μ respectively. The simple mouth opening has a single piercing tooth (Fig. 143*C*), and the vulva has a conspicuous flap over it; the male bursa (Fig. 143*D*) is very expansive and has a small, asymmetrically-situated dorsal lobe. Infected animals are usually treated with copper sulphate drenches.

A very similar worm, *Mecistocirrus digitatus*, distinguishable from *Hæmonchus* by its long slender spicules, inhabits the stomach and duodenum of cattle, sheep, and pigs in India and the Far East; there is one doubtful human record from Hong Kong.

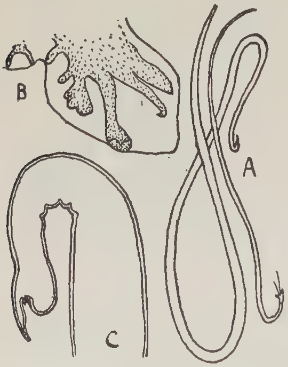

Fig. 144. *Metastrongylus apri.* *A*, male and female worms, × 3; *B*, bursa of male; *C*, posterior end of female. (*B* after Stephens, *C*, after Gedoelst.)

Metastrongylidæ. — The members of this family, with their slender bodies and position outside the digestive tract, might be confused at first sight with Filarioid worms. The males have small bursas with stumpy rays, while the females have the tail recurved against the posterior part of the body and terminated by a finger-like process. Most of them inhabit the fine branches of the bronchial tubes of the lungs of mammals, but one species lives in the heart and pulmonary arteries of dogs, and another has been found in the frontal sinus of the tiger. The eggs of the worms hatch in the lungs and the larvæ make their way to the throat and are usually swallowed, being passed in the feces. The infective larvæ which develop in a few days are said to be remarkably resistant to drying. They are not known to penetrate the skin, but enter the body by being swallowed. Presumably they reach their final destination in the lungs by way of the blood stream. Many species occur in ruminants, pigs, dogs and cats, and may produce serious lung diseases.

Only one species, *Metastrongylus apri* (Fig. 144), a common parasite of pigs, has been found in man, and this only three times. The females are about 20 to 50 mm. long and 400 to 450 μ in diameter, while the males are about half this size. The larvæ as found in the feces are distinguishable by the presence of a fine undulant appendage at the end of the tail. Attempts at treatment of lung worms in animals have been made by tracheal injection of various substances and by inhalation of chloroform, or fumes of tar, sulphur, etc.

CHAPTER XVII

OTHER INTESTINAL NEMATODES

In addition to the members of the suborders which have been considered in the preceding two chapters, there are three other nematodes which are very common and important human parasites, namely *Ascaris lumbricoides*, *Enterobius* (*Oxyuris*) *vermicularis*, and *Strongyloides stercoralis;* each one represents a separate suborder, — Ascaridata, Oxyurata and Rhabdiasata, respectively. There are also a number of other rare species of nematodes which are only of interest as curiosities. In connection with the intestinal nematodes it is convenient to consider also the spiny-headed worms or Acanthocephala.

Ascaris and Its Allies

There is no worm which more commonly inhabits the human body, or has a wider distribution in the world, and few which have been known to man for a longer time, than ascaris, yet, strangely enough, important details of its life cycle were unknown before 1916, and the factors influencing its epidemiology are only now being elucidated. One reason for this is the fact that ascaris infections have in general not been taken very seriously, and their injurious effects have been minimized, whereas the effects of hookworm have often been exaggerated. In recent years ascaris has begun to step into the limelight more and more as a really injurious and sometimes dangerous parasite. When a parasite steps into prominence nowadays it has little more chance to keep any details of its life and habits under cover than has a candidate for public office.

Ascaris lumbricoides is one of the largest nematodes. The females commonly reach a length of 8 to 14 inches, but may even get 18 inches long, and are 4 to 6 mm. in diameter. The males are 6 to 12 inches long, but distinctly more slender than the adult females; they are always distinguishable by the curled tail, whereas the females have a blunt tail. Both sexes are more slender at the head end.

In common with other members of the Ascaridata, *Ascaris lumbricoides* has the mouth guarded by three lips, one dorsal and two lateroventral, each with minute papillæ. The esophagus is nearly cylindrical, and is followed by a flattened, ribbon-like intestine. The vulva is situated about one-third the distance from head to tail. The coiled tail of the male is short and provided with a characteristic number and arrangement of papillæ, but no alæ. This worm is a very favorite object for the study of nematode anatomy, since it is always easily obtainable, and on account of its large size is easily dissected.

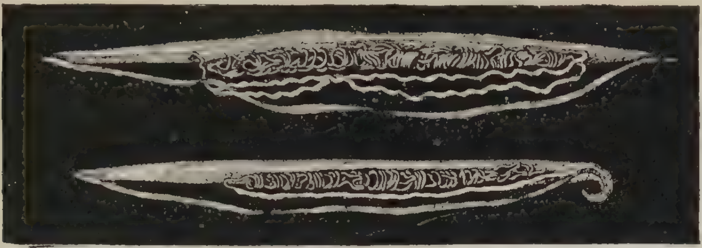

FIG. 145. *Ascaris lumbricoides*, dissected to show anatomy; female above, male below. Note ribbon-like intestine (cross-barred) with pharynx at its anterior end; the coiled thread-like ovaries in female and testis in male; the large kinky oviducts in the female, uniting to form a vagina near the external opening on the anterior third of the body; and in the male the large sperm duct opening at the ventrally-curved posterior end of the body in common with the intestine.

An ascaris which is indistinguishable morphologically or even serologically from the human species is a very common parasite of pigs, and up to the last few years these two have been regarded as identical, but recent work by several different investigators has shown that the eggs derived from pig ascaris do not ordinarily develop to mature worms in man, or vice versa, and that there is little epidemiological relationship between infection in these two hosts. It would seem preferable, therefore, to distinguish the pig ascaris as *A. lumbricoides*, var *suum*. There is no doubt but that in nature human ascaris infection ordinarily spreads from man to man, and that the pig is negligible as a host, though sometimes important as a disseminator of eggs on account of its fondness for feeding on human feces.

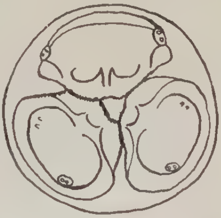

FIG. 146. Lips of *Ascaris lumbricoides*, end-on view. (After Yorke and Maplestone.)

The adult ascaris normally lives in the small intestine, where it is supposed to feed on the semi-digested food of the host, but there is evidence that it commonly bites the mucous membranes with its lips and sucks blood and tissue juices to some extent, as do hookworms. The egg production is astounding. Miss Cram (1925) estimated the number of eggs contained in a mature female worm to be as high as 27,000,000, and Brown and Cort (1927) and Augustine *et al.* (1928) have estimated that the eggs per gram of feces for each female worm is in excess of 2000. This would indicate a daily production of something like 200,000 eggs! Evidently the chances against the offspring of an ascaris reaching a comfortable old age in a human intestine are many millions to one.

The eggs (Fig. 147 *A* and *B*) are very characteristic, having a thick, clear, inner shell covered over by an irregular, warty, albuminous coat which is stained yellow or brown in the intestine; they usually measure about 60 to 70 μ by 40 to 50 μ. Unfertilized eggs are more difficult for a beginner to identify, since they are more elongate and less regularly oval in shape, and have amorphous contents instead of the well-defined round cell of the fertilized eggs.

Life Cycle. — When they leave the host the eggs are unsegmented. In order to develop they require a temperature lower than that of the human body, at least a trace of moisture, and oxygen. They are extremely resistant to chemical substances, and can be successfully cultured in 1% to 2% formalin; even such substances as strong acids and alkalies, copper sulphate, and petroleum do not kill them. They are, however, killed by immersion in water at 130° F. in one minute, and at 122° in 45 minutes. They gradually degenerate at temperatures above 100° F. and cease development below about 60°; about 85° is the most favorable temperature. Martin (1926) found eggs capable of causing infection after storage for 4 years in an ice box. Absence of oxygen retards or stops development, while complete drying not only stops development but is lethal. According to Otto (1929) eggs of ascaris from man and pig will develop in dry soil in a saturated or nearly saturated atmosphere at a temperature of about 72° F., but die when the relative humidity falls below 80%. At higher temperatures more moisture is required. Dried female ascarids kept by Martin in a bottle in an ice box contained eggs which developed at the end of at least 25 months. The investigations of Otto (1929), the Caldwells (1928), and Brown (1927), however, show that, contrary to earlier opinion, ascaris eggs degenerate when exposed to a combination of heat and dryness. Eggs in feces passed on sandy soil exposed to the sun in a hot climate all die before the embryos can develop, on account of the high temperatures generated; in other soils where moisture is retained better and the temperature held down by evaporation, the sun is not so injurious. The writer's observations in India showed that while ascaris was very prevalent in the wet parts of eastern India, with abundant moisture and shade, it was non-existent in the hot dry parts of western India.

Under favorable conditions of temperature, moisture and air the eggs develop active embryos within them in from 10 to 14 days, though under natural conditions the majority of the eggs require about three weeks.

Although Maplestone suggests the possibility of infection taking place by larvæ which hatch from the eggs under some so far unknown conditions outside the body, so far as known at present infection normally occurs from the swallowing of embryonated eggs. The writer was able to show that in some places in India heavy infection was directly correlated with polluted water supplies, but that in other localities the water could not be involved. Brown (1927) observed the same thing in Panama, and discovered that there the infection was of household nature, and was presumably obtained from soil on the floors and door yards of huts polluted by young children. Such stools are ordinarily swept up and enough fecal material is left to seed the soil heavily with ascaris eggs. A similar condition exists in Bengal. Prenatal infection from eggs eaten by the mother is also possible.

When the eggs are swallowed the embryos hatch in the small intestine. It was first discovered by Stewart (1916) that these embryos did not develop directly to maturity in the intestine, but first go on a ten-day tour, a sort of home-seeker's trip, through the body in the same manner as do hookworms. They penetrate the mucous membranes and are carried by the blood stream to the liver, then the heart and then the lungs. Here they burrow out and make their way through the trachea, throat and esophagus back to the intestine, meanwhile having benefited from the trip by a growth from an initial length of about 200 to 300 μ to about ten times this length (Fig. 147*C*). The migration through the lungs takes place readily in rats, mice, guinea pigs and other rodents as well as in the natural hosts, but after the return to the intestine the worms pass right on through in unnatural hosts, and are voided in the feces. Even in natural hosts, experimental infection with thousands of eggs, although it sets up a severe pneumonia, results in the establishment of only a very small percentage of the worms in the intestine, and sometimes none at all. It is possible that the heavy experimental infections, by causing fever and stimulating whatever immune reactions the host is capable of, may be unfavorable for the final establishment of the worms, whereas the occasional ingestion of two or three eggs, such as would occur in nature, might enable a large number of worms to "sneak in," as it were, in the course of time. After reaching the intestine, the young worms, 2 to 3 mm. long, grow to maturity in 2 to 2½ months.

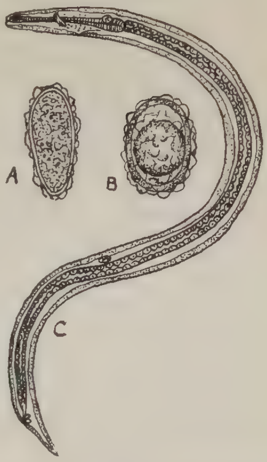

FIG. 147. *Ascaris lumbricoides.* *A*, infertile egg; *B*, fertile egg; *C*, larva from lung of rabbit 10 days after infection. × about 65. (After Ransom and Foster.)

Pathology. — In heavy experimental infections the migration of the larvæ through the lungs causes hemorrhages, and sets up a severe pneumonia which may be fatal. Smirnow and Glasunow (1928) have observed that the invasion is accompanied by a fever, a temporary anemia and leucocytosis, and an eosinophilia. Pigs in nature frequently show lung symptoms, known as " thumps," and similar conditions have been observed in human beings preceding an ascaris infection; ordinarily in nature, however, not enough eggs are ingested at a time to cause serious pneumonia.

After reaching maturity in the intestine, ascaris may or may not disturb the peace of the host. Numerous cases of light infections are entirely unsuspected until the eggs are found in the feces. On the other hand the parasite is not always so docile. In heavy infections the worms are likely to tangle themselves in masses, especially if made uncomfortable by some food or drug taken by the host, and completely block the intestine. Cases are on record of from 1000 to 5000 worms being present, but even less than a hundred worms may cause a blockage which is fatal if not surgically removed. A number of cases of death after carbon tetrachloride treatment for hookworm are known, due to intestinal obstruction of the intestine by squirming masses of irritated ascaris. The worms sometimes irritate the mucous membranes so much by their excretions that they cause dangerous spasmodic contractions or permanent nervous constrictions of the intestine. They also sometimes cause appendicitis by blocking the appendix. Other symptoms are caused by toxic substances which cause effects resembling anaphylactic shock, and others which poison the nervous system, producing such symptoms as convulsions, delirium, general nervousness, coma, etc. Stunting of growth has been demonstrated in pigs and dogs, and very likely occurs in man also; in fact some Japanese workers recently found that ascaris-infested school children were shorter than the uninfected ones, and "had less memory and thinking capacity." Simonin (1922) has collected clinical evidence of serious effects on glands of internal secretion.

The list of dangerous complications of ascaris infection is greatly enlarged by the fact that the worms have a "wander-lust," and tend to explore ducts and cavities. They occasionally creep forward and emerge from the nose or are vomited by the horrified patient, or they may cause suffocation; they invade bile ducts, and more rarely pancreatic ducts, and block them or wander into the liver tissue; they pass through the intestinal wall and cause fatal peritonitis, or may even come through the umbilicus or groin; and they may make their way into the pleural cavity, urinogenital organs, etc. It is evident, therefore, that these worms, so far from being the "guardian angels" of children, as they were once considered, are more like bulls in a china shop.

Treatment and Prevention. — Ascaris, as long as it stays in the intestine, is usually fairly easily expelled by either chenopodium or santonin, but sometimes inadequate treatment, by merely irritating the worms, makes matters worse, and it is seldom possible to reach them, except by surgery, when they have migrated to places where they do not belong.

Prevention must depend on improved sanitation. All of the factors involved in the transmission are not yet known, but it is evident that the main dependence must be placed on clean drinking water, avoidance of possibly contaminated vegetables, especially if fertilized with night-soil, prevention of children from polluting the soil in the immediate vicinity of habitations, and protection of food from flies.

Other Ascaridata. — In addition to the pig ascaris, there are several other members of the same family found in domestic animals, some of them rarely in man. *Ascaris vitulorum* is a parasite of calves, and *A. equorum* (*megalocephala*) of horses. The related genus *Toxocara*, which has cervical alæ giving the anterior end an arrow-head shape, contain the common ascarids of dogs and cats. *Toxocara canis* is the common ascaris of dogs, and *T. mystax* (*Besalcaris cati*) (Fig. 148) of cats. The latter species has been recorded 9 times in man. The males of this species are about 2 inches, and the females 3 to 4 inches, in length. Another rare ascarid found in man is *Lagochilascaris minor*. This is normally an inhabitant of the intestine of the cloudy leopard. In several cases in Trinidad and Guiana sexually mature specimens have been found in subcutaneous or tonsillar abscess about the head. The abscesses last for years, discharging pus and small worms several millimeters in length. The adults are about the size of hookworms, and are identifiable by their lips and a keel-like expansion of the cuticle extending the whole length of each side.

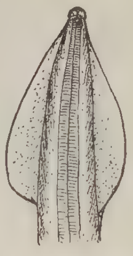

FIG. 148. Head of *Toxocara mystax*, showing cervical alæ.

Worms of a related family, Heterakidæ, which have a preanal sucker and, in the males, conspicuous caudal alæ, are important parasites of the large intestine of poultry.

Oxyuris and Its Allies

The majority of the members of the human race, even in highly sanitated countries, fail to get through life without affording food and shelter for oxyuris, also popularly called the seat worm or pin worm, (*Enterobius* *vermicularis*). These little white worms so often seen wriggling actively in freshly passed feces, are cosmopolitan in distribution; they occur only in man, although closely related species are found in apes and monkeys.

Structure and Life Cycle. — The adult worms live in the cecum, appendix and neighboring parts of the intestine. The females, which are the only forms usually seen, are often mistaken for hookworms by people who have read about these but have never seen them. Like other members of its suborder, the worms have rather transparent body walls through which the internal organs can be seen. They have an esophagus with a conspicuous bulb at its posterior end, and three very small lips; the head is surrounded by a bulbous swelling of the cuticle. The females, 8 to 13 mm. long, have a body which tapers to more or less of a point at each end, but the tail end is very finely drawn out, and accounts for nearly one-third of the length. The vulva is anterior to the middle of the body. The minute males, which are only 2 to 5 mm. long and 100 to 200 μ broad, are much less numerous than the females, and are seldom noticed. The tail is curled and has a small bursa-like expansion, and there is only one spicule.

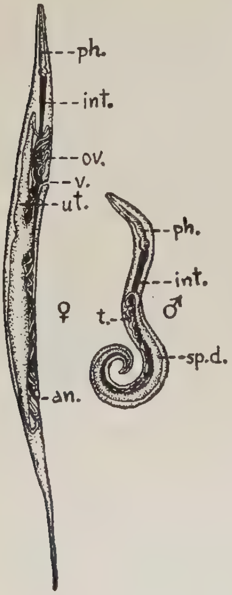

FIG. 149. Pinworm, *Enterobius vermicularis;* ♀, female; ♂, male; *ph.*, pharynx; *int.*, intestine; *ov.*, ovary; *ut.*, uterus; *an.*, anus; *v.*, vulva; *t.*, testis; *sp. d.*, sperm duct. × 8. (After Claus, from Braun.)

As the uteri of the females fill with eggs, the worms release their holds in the intestine and either pass out of the body with the feces or voluntarily migrate out of the anus, sometimes entering the vagina, causing intense itching in the process. The contact with air stimulates the worms to deposit eggs, and a trail of these is left behind as the worm crawls, though eggs are only exceptionally found in the fresh feces before the worms have disintegrated. Eventually the body dries and explodes, liberating all the remaining eggs in showers. The eggs when first laid contain partially developed embryos, in the "tadpole" stage (Fig. 150*A*); they quickly mature but remain in the egg shell until swallowed. The eggs are clear and unstained, measuring about 55 by 30 μ, and are flattened on one side.

The eggs regain access to the same or another person in various ways, but probably usually by way of the hands. The itching caused by the emigration of the worms from the anus results in scratching, especially at night, and the eggs lodged under the finger nails may eventually reach the mouth in children or others who are careless in their habits. They may also get to the fingers from night clothes or bed linen, and in other possible ways. Some of the cases of long duration are difficult to explain, and it has been suggested by some, who have found adult, eggs, and larvæ simultaneously in the intestine, and a periodicity in the appearance of worms in the stools, that the worm may multiply generation after generation in the intestine of its host; but Zawadowsky and Schalimov (1929) have shown that this cannot happen, for the eggs will not develop beyond the "tadpole" stage in the absence of free oxygen. These authors also demonstrated that the eggs are incapable of development outside the uteri of the parent worms if they have not already reached the "tadpole" stage, due to the fact that there is an inner protective membrane of the egg, highly impervious to water and chemicals, which does not "ripen" until this stage of development is reached. Before this "ripening" has occurred the egg is not sufficiently protected against environmental factors to be able to survive outside the uteri of the mother worm.

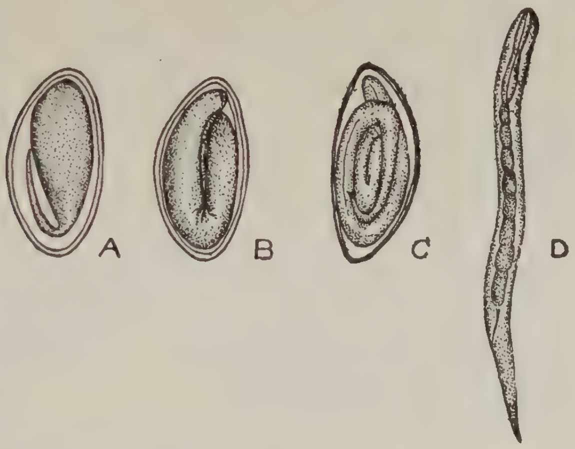

FIG. 150. Early development of pinworm, *Enterobius vermicularis*. *A*, newly laid egg containing tadpole-like larva; *B*, egg 12 hrs. later with nematode-like larva; *C*, egg with fully developed embryo; *D*, newly hatched embryo. × 500. (*A* and *B* after Braun; *C* and *D* after Leuckart.)

Pathology. — The itching caused by the worms as they migrate from the anus and between the buttocks, which may be intense, may cause loss of sleep and lead to nervousness, and even to sexual disorders. Inside the intestine, the mucous membranes of the cecum may be seriously inflamed, causing digestive disturbances and reflex nervous symptoms. No doubt absorption of toxins also contributes to nervous symptoms, such as insomnia, epilepsy, fidgetiness and the like, as well as to occasional instances of anemia. Many people believe that oxyuris is a common incitant of appendicitis, whereas others think the evidence for this is far from convincing. Harris and Browne (1925) found this worm in the appendix in 22 cases out of 121 appendicitis operations, and they think the worm would be found more frequently by others in such cases if looked for.

Treatment and Prevention. — Treatment is difficult on account of the position of the worms far back in the digestive tract. Nearly all of the nematode group of anthelmintics, especially thymol, chenopodium and carbon tetrachloride, expel some worms, but not all. Often good results can be obtained by the use of enemas if so administered that they get far back in the colon. An enema of carbon tetrachloride in warm milk was found by the writer to give good results. Applications of ointments on anal bandages are useful in preventing reinfection, and unless reinfection occurs the infection should clear up in two or three weeks.

The infection tends to spread in families and among children in school, and can only be stopped by measures to keep the hands from becoming infected, — by anal bandages and frequent and thorough washing of hands, and by preventing contamination of towels, bed linen, etc., by infected persons.

Other Oxyurata. — The only domestic animal which suffers from oxyuris infection is the horse, which harbors a large species known as *Oxyuris equi.* Rodents harbor numerous species, and one of these, *Syphacia obvelata* of mice and rats, was found once in a child in the Philippines. Its eggs are shaped like those of *Enterobius*, but are 110 to 142 μ long. Common oxyurids for class study can nearly always be found in large cockroaches.

Strongyloides and Its Allies

The smallest worms parasitic in the human body, except the male trichina, is *Strongyloides stercoralis.* This parasite is further unique in that there are no males — only parthenogenetic females (or possibly hermaphrodites) — in the body of the host, and that under favorable conditions outside the body there may be an alternating generation of free-living males and females which do not at all resemble the parasitic females. These worms, together with some forms with the same type of life cycle found in amphibians and reptiles, are now placed in a suborder of their own, Rhabdiasata.

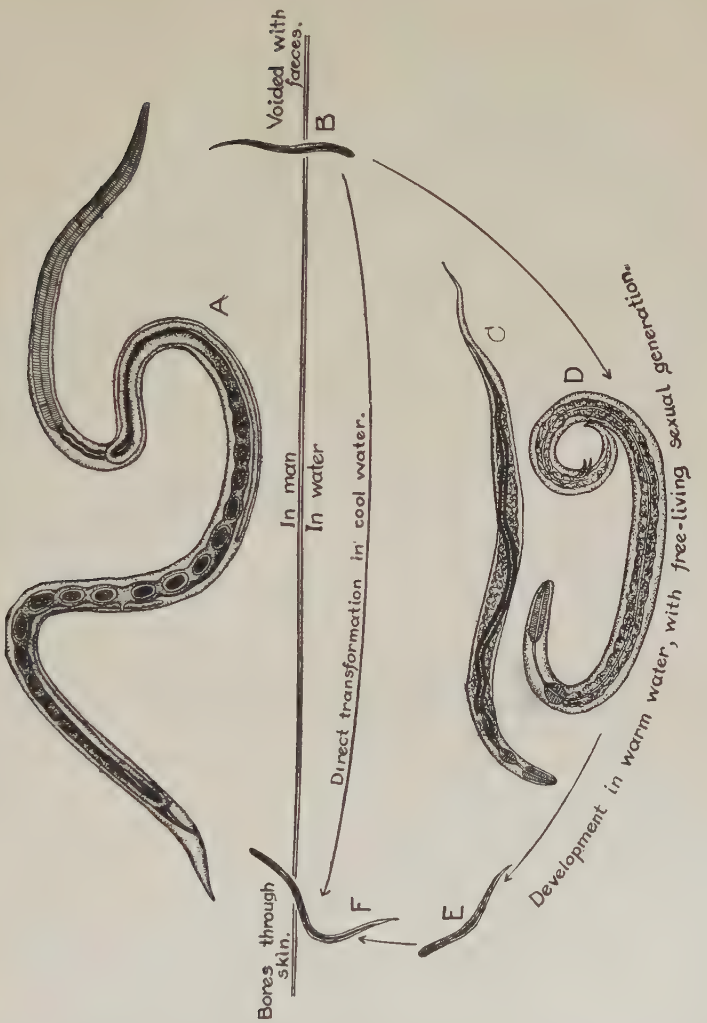
Voided with faeces.
B
A
In man
In water
Direct transformation in cool water.
C
D
Development in warm water, with free-living sexual generation.
E
F
Bores through skin.

FIG. 151. Life history of *Strongyloides stercoralis.* *A*, adult female in intestine (note long pharynx, egg-containing uterus, and vaginal opening on posterior third of body; *B*, newly born embryo as passed with feces; *C* and *D*, adult female and male, respectively, of free-living generation; *E*, "rhabditiform" larva, from female of free-living generation; *F*, filariform larva, formed by metamorphosis of *E*, ready to infect by boring through skin. × 75. (Partly after Looss.)

Strongyloides stercoralis is undoubtedly far more common, especially in the tropics, than statistics based on ordinary stool examinations would indicate. Culture methods of diagnosis have shown that in some parts of India the infection rate cannot be less than 10%. The available epidemiological evidence indicates that the parasite thrives best in locations with a heavy annual rainfall.

The parasitic females of *Strongyloides stercoralis* are slightly over 2 mm. in length with a diameter of only 40 to 50 μ, and so are barely visible to the naked eye. The posterior part of the body is occupied by the relatively large eggs, measuring about 50 by 32 μ, some of which may be already hatched by the time they leave the vulva.

The eggs, containing developed embryos when deposited, usually hatch almost at once in the intestine of the host, but occasionally are carried out in the feces unhatched. The embryos closely resemble those of newly hatched hookworms except that they have a very short gullet leading into the double-bulbed esophagus. If large numbers of larvæ and few or no eggs are found in *fresh* feces, there is no question but that it is a Strongyloides and not a hookworm infection. Even in stale feces the unhatched eggs of hookworms are more numerous than hatched embryos.

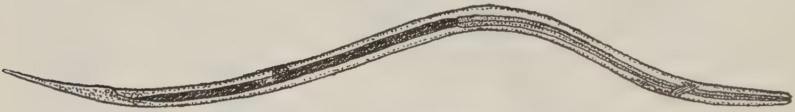

Fig. 152. Mature "filariform" larva of *Strongyloides stercoralis*. × 180. (Modified from Looss.)

The embryos, after leaving the host's body, pursue one of two courses of development; they either grow and transform into "filariform" larvæ directly, or they first develop into reproducing males and females which in every respect resemble free-living nematodes such as *Rhabditis*. This may occur within 30 hours. These free-living adults, about 1 mm. in length and 40 to 60 μ broad, produce eggs precisely as soil nematodes do, and these hatch into embryos like those passed in the feces, which subsequently transform into the same kind of "filariform" larvæ (Fig. 152). The factors which determine which mode of development is followed have not yet been determined. The filariform larvæ appear in the cultures in less than 48 hours by direct development, and become progressively more numerous up to about a week by reproduction of the free-living generation. They are about 600 μ in length with a diameter of 16 to 17.5 μ, and are at once recognizable by the long, filiform esophagus, which occupies over 40% of the body length. The subsequent history of the parasite up to maturity in the intestine is practically identical with that of hookworm larvæ. The habits of the infective larvæ are similar, and the penetration of the skin and course in the body are identical, except that, according to Fulleborn, the migratory course through the lungs is not optional but necessary.

In view of the persistency of Strongyloides infections — Fulleborn cites one case of 24 years' duration — it has long been suspected that auto-infection occurred. Fulleborn found evidence of self-infection through the skin in the region of the anus, from larvæ which adhered there in minute traces of feces long enough to change into filariform larvæ. More recently Nishigori has obtained evidence that the young larvæ in the intestine, if retained more than 24 hours, can transform into filariform larvæ, penetrate the intestinal wall, and cause re-infection after going through the liver, heart and lungs; he considers constipation an important factor in auto-infection.

Pathology. — There is much difference of opinion about the injuriousness of Strongyloides infections. There is no doubt but that many individuals, particularly negroes, harbor even very heavy infections without evident symptoms. On the other hand, there is much clinical evidence of an intermittent chronic diarrhea, sometimes of very intractable type, in cases in which no other cause for the symptoms can be discovered, and Sandground (1926) has obtained evidence of these symptoms in experimentally infected dogs, clearly associated with the Strongyloides infection. The worms burrow deep into the mucous membranes and even the submucosa of the intestine, and both they and their offspring set up considerable irritation. According to Nishigori, repeated auto-infection may give rise to chronic symptoms of peritonitis, bronchitis or even pneumonia. Symptoms of anemia and eosinophilia, sometimes accompanied by other evidences of general intoxication, have frequently been observed, and are attributed to absorption of toxic products, either from the worms or of bacterial origin, through the lesions in the intestinal wall in individuals who do not have the power, as some apparently have, of neutralizing these poisons and rendering then innocuous.

Ordinary anthelmintic treatment is of no avail, but de Langen (1929) states that infections can be cured by intravenous injection of tartar emetic, accompanied by gentian violet by mouth. Prevention of fresh infection depends on the same measures as are applicable in the case of hookworm, but continuous auto-infection can only be controlled by careful cleanliness after defecation and, if Nishigori's work is confirmed, by care in avoiding constipation.

Other *Strongyloides* and Related Worms. — *S. stercoralis* is infective for dogs and cats as well as man, but usually dies out in a number of weeks. In India, however, the writer found a high percentage of cats to be naturally infected with a Strongyloides which was very similar to, if not identical with, the human species. Other species occur in monkeys, sheep, rodents, pigs and other animals. Most of the species in herbivorous animals, if really more than varieties of *S. papillosus* of sheep, differ from those in man and carnivores in that the eggs do not usually hatch until after they have left the body of the host.

Undoubtedly related to Strongyloides, but differing in that there is no parthenogenetic (or hermaphroditic) generation, are the species of *Rhabditis*. These are normally free-living nematodes living in soil, decaying matter, or water, but occasionally some of them are able to establish themselves temporarily in the human body. *R. pellio* is a species which has on a few occasions been found living in the vagina, the larvæ escaping in the urine. Another species, *R. hominis*, has been recorded both from Japan and the United States in stools of man and animals. The worm is undoubtedly not a true parasite; eggs ingested with foods or water may possibly develop into larvæ or adults before being evacuated, but in most instances the worms contaminate the feces after they are passed and rapidly multiply in them. Their only importance is the frequency with which stools containing them are diagnosed as containing Strongyloides. Cultures fail to produce the characteristic filariform larvæ of the latter worm.

In India the writer found, in a total of seven cases, feces containing eggs like those of *Rhabditis*, measuring about 55 by 28 μ, which were in stages of segmentation and produced " rhabditiform " larvæ in cultures, but did not produce either filariform larvæ or sexually mature adults. Their true nature is unknown.

Spiny-headed Worms (Acanthocephala)

In connection with the intestinal nematodes there should be mentioned the occasional occurrence in man of at least two species of Acanthocephala which, as noted on p. 291, are only distantly related to the true nematodes. Their ugly spiny proboscides, by means of which they adhere, and the complete absence of a mouth or digestive tract, as well as the peculiarities of their internal structure, make them easily recognizable.

The common spiny-headed worm of rats, *Moniliformis moniliformis* (Fig. 153) has been found in man on a few occasions. Its body, 4 to 10 inches long in females and about 2 inches long in males, has annular rings which give it a tapeworm-like appearance. It has a nearly cylindrical proboscis with 12 to 15 rows of vicious thorn-like hooks. It inhabits the small intestine of rats in many parts of the world, but in most places is not common. In Houston, Texas, however, the writer found them in about 20% of the roof rats (*Rattus alexandrinus*), a very common species there, but in a much smaller percentage of Norway rats. The eggs, which are over 100 μ in length, contain developed embryos provided with hooks. Cockroaches serve as intermediate hosts; the writer has found upwards of 100 encysted larvæ in the body cavity of a *Periplaneta americana*. In Europe a beetle has also been involved. Roof rats feed extensively on roaches and roaches on the droppings of rats. Human infection, of course, can only occur when infected roaches are eaten, accidentally or otherwise.

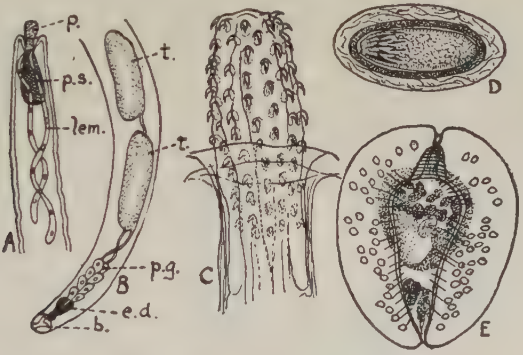

Fig. 153. *Moniliformis moniliformis*. *A*, anterior end of worm; *B*, posterior end of male; *C*, proboscis; *D*, egg; *E*, larva extracted from cyst in cockroach; *e.d.*, ejaculatory duct; *b*, bursa; *lem.*, lemniscus; *p.* proboscis; *p.s.*, proboscis sac; *p.g.*, prostate or cement glands; *t.*, testes. (*A*, *B* and *E*, after Travassos; *C*, after Van Cleave; *D*, original.)

The only other spiny-headed worm which has been recorded from man is the relatively huge species, *Macracanthorhynchus hirudinaceus*, commonly parasitic in pigs. This large worm, of which the females are 12 to 18 inches long, though the males are only 2 to 4 inches, is pinkish in color and has a transversely wrinkled body which tapers from a rather broad, rounded head end to a slender posterior end. The proboscis is relatively very small, like a little knob at the head end, and is armed by 5 or 6 rows of thorns. The eggs, with characteristically marked brown shells, are 80 to 100 μ long, and contain embryos with hooks. The intermediate hosts are various species of white grubs, the larvæ of "June-bugs" and related beetles. Lindemann (1865) recorded this worm as parasitic in man, and stated it to be common among the peasants of the Volga Valley in Southern Russia, where the white grubs of beetles are said to be eaten, but there are no subsequent confirmations of this. Lambl, in 1859, found an immature Acanthocephalan in a boy in Europe, which probably was this species.

CHAPTER XVIII

FILARIÆ AND THEIR ALLIES

(SUBORDER SPIRURATA)

All of the nematodes which have been considered in the preceding pages are transmitted directly from one host to another, either as eggs or larvæ, without the intervention of an intermediate host. In the suborder Spirurata, however, we come to a group all the members of which, so far as known, take advantage of intermediate hosts as a means of gaining access to another individual of the final host species.

This large group of nematodes is divided into three superfamilies. One, the Dioctophymoidea, contains a few peculiar worms of medium or very large size inhabiting the kidneys, glands, or other extra-intestinal parts of birds and mammals. They have no lips, the female has only one ovary, and the male has a muscular bell-shaped bursa with no rays, and a single spicule. Although Faust places these worms with the Spirurata, there is no general agreement as to what their real affinities are. The superfamily Spiruroidea includes a host of worms inhabiting various parts of the alimentary canal or its walls, or other parts of the body. Most of them have two or four lips and often a chitinous vestibule; the females usually have the vulva in the middle or posterior part of the body, and the males have a spirally coiled tail usually with conspicuous alæ supported by papillæ (see Fig. 168). In most cases the eggs or larvæ escape with the feces, are eaten by coprophagous insects, and regain access to a new host when these are swallowed. The superfamily Filarioidea include mostly slender thread-like worms which inhabit some part of the blood or lymphatic system, connective tissues, or such internal cavities as the abdominal cavity, eye sockets, nasal cavities, etc. They have simple mouths without lips and rarely a vestibule; the females nearly always have the vulva far forward near the mouth, and the relatively small males have spirally coiled tails, with or without alæ, but always with papillæ. They produce living embryos which usually swarm in the blood or skin and await release by blood-sucking insects; from these, after they have undergone partial development corresponding to the free-living stage of hookworms, they regain access to a new host while the intermediate host is sucking blood. In one instance, however, (the guinea-worm) the female takes the expulsion of the larvæ into her own hands, and deposits them through the skin into water, where they infect Cyclops which are subsequently swallowed with drinking water.

The observation of the development of the larvæ of filariæ in mosquitoes, first observed by Manson in China in 1878, as the result of his suspicion that the nocturnal larvæ were probably in the blood for some purpose and were very likely liberated by a nocturnal blood-sucking insect, was the first demonstration of the rôle of blood-sucking insects in the transmission of disease, and marked the beginning of a new era in modern preventive medicine.

Many filarial infections are practically impossible of diagnosis except by the embryos or "microfilariæ," and it is therefore important to be able to distinguish them. When living they are colorless and transparent, and may or may not be enclosed in "sheaths." In order to identify them it is usually necessary to stain them. The body will then be found to contain a column of nuclei, broken in definite places which serve as landmarks (Fig. 154). The principal ones are a nerve ring anteriorly, an excretory pore or "V" spot, an excretory cell somewhat further back, a few genital cells posteriorly, and an anal pore or "tail spot." The spacing of these landmarks is fairly constant in different species. The presence or absence and arrangement of nuclei in the head and tail ends, and the shape of the tail, are also useful identification marks. The following table shows the outstanding characters of the microfilariæ found in human blood or skin (see also Fig. 155).

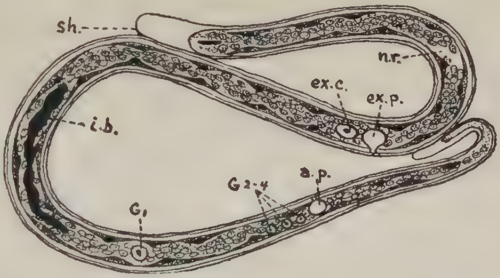

FIG. 154. Anatomy of a microfilaria, *Mf. bancrofti;* *a.p.*, anal pore or "tail spot"; *ex.c.*, excretory cell; *ex.p.*, excretory pore or "v" spot; *i.b.*, "inner body"; G_1, G_{2-4}, genital cells; *n.r.*, nerve ring; *sh.* sheath. × 600. (After Fulleborn.)

Sheathed forms.

Mf. bancrofti: about 300 μ by 10 μ; sheath stains red with dilute Giemsa stain; tail end tapers evenly; no nuclei in tail; does not stain with 1 : 1000 methylene blue when alive; lies in graceful coils when dried; nocturnal or non-periodic, in blood or urine.

Mf. loa: same size; sheath unstained in Giemsa; tail short and recurved, with nuclei to tip; stains with methylene blue when alive; lies in kinky scrawls when dried; diurnal, in blood.

Mf. malayi: about 230 μ by 5 to 6 μ; tail sharp-pointed, with a single nucleus at its tip and another 10 μ in front of it; nocturnal.

Unsheathed forms.

Mf. perstans: about 200 μ by 4 μ; tail ends bluntly, with nuclei to its tip; stains with methylene blue when alive; no periodicity; in blood.

Mf. streptocerca: about 215 μ by 3 μ; tail ends in a crook, and terminates bluntly with nuclei to tip; does not stain with methylene blue when alive; no periodicity; in skin.

Mf. ozzardi: about 200 μ by 5 μ; tail sharply pointed, with no nuclei at its tip; stains with methylene blue when alive; no periodicity; in blood.

Mf. volvulus: about 300 μ by 5 to 8 μ; tail sharply pointed, with no nuclei at its tip; no periodicity; in skin.

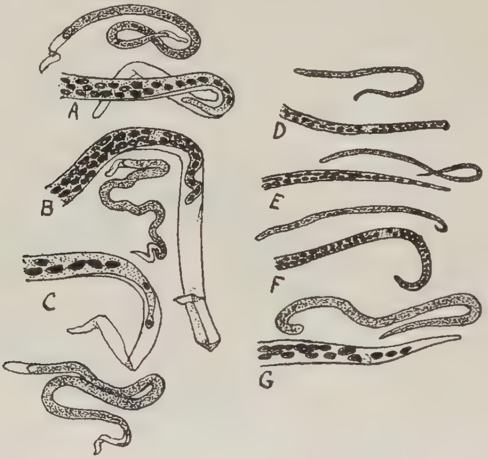

FIG. 155. Tails of various microfilariæ of man. × 600. Relative size of adults also shown, × about 200. (Adapted from figures by Fulleborn) *A*, *bancrofti* (sheathed; tip of tail without nuclei); *B*, *loa* (sheathed; nuclei to tip of tail); *C*, *malayi* (sheathed; one nucleus at tip of tail, one 10 μ forward); *D*, *perstans* (no sheath; tail blunt, with nuclei to tip); *E*, *ozzardi* (no sheath; tail sharply pointed, no nuclei at tip); *F*, *streptocerca* (no sheath; tail always hooked, nuclei almost to tip); *G*, *volvulus* (no sheath; size large, no nuclei in end of tail).

Wuchereria (*Filaria*) *bancrofti*

This worm, which is usually referred to merely as " filaria," is a very common and very important human parasite. It has a wide distribution throughout the warm parts of the world, especially in moist low-lying areas of sea coasts and river valleys. The infection is particularly prevalent in parts of Bengal and the southwest coast in India, many localities in southeastern Asia, China, the East Indies, and South Sea Islands, in a large part of Africa, especially on the tropical east and west coasts, in Queensland, and in many parts of the West Indies and tropical America. In the United States there is only one endemic locality, — Charleston, South Carolina. In some of the localities mentioned over

50% of the inhabitants have the embryos of this filaria swarming in their blood, and there are localities where a large majority show diseased conditions which are attributed to the infection. Lane (1929) thinks it not unlikely that the ancestral home of the worm was in Oceania, whence early explorers from the archaic civilization of the Near East, going east in pursuit of gold and pearl shell, brought the worm and the taro plant back with them to India and Egypt, just as later the European civilization, searching America for gold, brought back the potato and syphilis to Europe, and left filaria and hookworm in their wake.

Structure and Life Cycle. — The adult worms (Fig. 156) live in the lymph glands or ducts, often in inextricable tangles, like white horsehairs. The females are 3 to 4 inches long, and only one-fourth of a millimeter in diameter — about the calibre of coarse sewing thread; the males are about half this size. The body tapers to a fine head slightly swollen at the end, with a simple pore as a mouth. The esophagus is partly muscular and partly glandular, with the vulva opening a little behind its middle. The males have the tail coiled like the tendril of a vine, with numerous pairs of papillæ; there is one long and one short spicule.

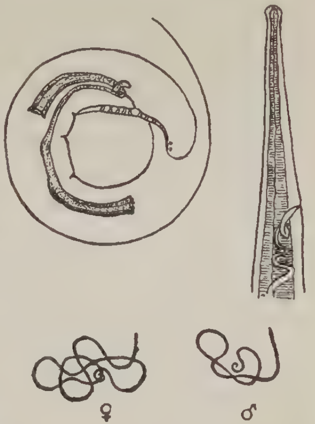

Fig. 156. Head of female and tail of male of *Wuchereria bancrofti*. Note slightly bulbous head, position of vulva, relative size of spicules, and arrangement of papillæ on a narrow ala. Beneath is shown the natural size of the male and female worms. Head, × 60; tail, × 15. (Adapted from Maplestone.) (Adult worms, natural size, after Manson.)

The female worms give birth to living embryos, called microfilariæ, which are surrounded by a delicate membrane, really the inner lining of the egg, for the eggs are never provided with a shell; this is commonly spoken of as a "sheath," and helps to distinguish the microfilariæ of this species from some others which do not have a sheath. The embryos measure about 300 μ in length and 8 to 10 μ in breadth, with blunt heads and rather pointed tails; the sheath fits like a glove over a finger, but is too long for the animal and can be seen projecting as a delicate membrane at the ends. It probably serves a useful function in keeping the writhing embryos from penetrating the walls of the blood-vessels and perversely exploring into places where they can have no hope of salvation.

The further development of the microfilariæ depends on their being ingested by certain species of mosquitoes which serve as nurses (see

p. 576). In Oceania the most important transmitter is *Aëdes variegatus* (*pseudoscutellaris*) which has habits similar to the yellow fever mosquito. In most other parts of the world the common nocturnal house mosquito of the tropics, *Culex quinquefasciatus* (*fatigans*), plays the leading rôle, whereas in China, according to Lee (1926), *C. pipiens* is the rascal; many other mosquitoes are capable of nursing the worms to the infective stage but are of minor importance in nature.

One of the most interesting and puzzling facts about the microfilariæ in the blood is their "periodicity," *i.e.*, their periodic appearance at night, chiefly from 10 P.M. to 4 A.M., in the peripheral blood, and their almost complete disappearance in the daytime. This happens in most parts of the world, but in Oceania, where the main transmitter is the day-biting *Aëdes variegatus*, there is no periodicity. The stimulus which times the appearance of the embryos in the blood is in some way connected with cessation of activity on the part of the host, for it is gradually reversed in people who sleep by day and work by night; yet sleep itself is not the factor, since the embryos begin to appear before the usual sleeping hours.

Two general hypotheses have been proposed to explain the periodicity of microfilariæ, but there are excellent arguments against either, and the phenomenon is still a mystery. One hypothesis assumes that the embryos are long-lived, and hide away somewhere in the interior of the body by day and come out into the skin capillaries at night, to keep a sort of tryst with their night-biting transmitter, *Culex*. It has been suggested that the embryos either retire to the larger internal vessels or are held in the capillaries of the lungs and other internal organs, either by contractions of the capillaries or by a coiling or twisting of the body to keep them from passing through. Many years ago Manson examined an infected suicide case six hours after a morning death, and found the microfilariæ very unevenly distributed, and especially numerous in the lungs. The long life of microfilariæ is supported by an experiment of Fulleborn's, in which a dog which he inoculated with embryos of *Dirofilaria repens* still harbored living embryos at the end of 2¾ years. This filaria, however, is a "non-periodic" species, a fact which may or may not have any significance. On another occasion Fulleborn injected a dog with blood containing 250,000 of the periodic *Microfilaria loa* and 20,000 of the non-periodic *Mf. perstans*. Only three of the former were ever seen again, whereas the latter persisted for two months. Little data is available with respect to *Mf. bancrofti*. It is claimed that the embryos disappear from citrated blood kept at body temperature within 22 hours, although they live for 3 days at room temperatures. When injected into an ape they are said to disappear forthwith, but Fulleborn found them alive for 10 days after injection into the body cavity of a mouse. Lane (1929), commenting on this hypothesis, remarks that in the absence of any method of adhering, the embryos have as much chance of staying in a large blood-vessel as a man would have swimming against the current half way down Niagara Falls; that if the embryos are held by contraction of capillaries, the contraction effects in a person simultaneously infected with the nocturnal *Microfilaria bancrofti* and the diurnal *Mf. loa* are too harassing to think about; that if, as estimated, a female *W. bancrofti* daily pours 2,000,000 embryos into the blood, the traffic conditions in the blood and lymph vessels in a man harboring even one reproducing worm would soon become rather congested; and that there is, after all, no sound evidence that the embryos have any secret hiding place, or any biological reason why they should have.

The alternative hypothesis is that the larvæ live less than 24 hours and that their birth is timed by some unidentified stimulus to take place at night. The implied daily disintegration and lysis of 2,000,000 embryos is not unreasonable when it is remembered that over two million million blood corpuscles are believed to be disposed of daily, and that a tiny tear can dissolve 5000 million bacteria in a few moments. Dead and dissolving microfilariæ have been observed in the body in large numbers, especially in the kidneys, which Fulleborn refers to as a veritable microfilarial cemetery. Manson's observation of abundant embryos in the lungs after death might be explained by the emptying of the uteri of the worms at the death of the host, in which case they might be expected to lodge in the lungs. The equally periodic appearance of microfilariæ in the urine in cases of chyluria, where they are blocked from entrance to the blood stream, is also circumstantial evidence in favor of periodic birth. Biologically, as Lane shows, this theory is reasonable. In Oceania, where *Aëdes variegatus* is the intermediate host, there is no periodicity — probably the primitive condition. This mosquito nurses to maturity a high percentage of the embryos it ingests unless killed by them. But in other places *Culex* takes over the transmitting rôle, and in this mosquito only a small percentage of the embryos succeed in developing to the infective stage. What more natural, then, than that there should evolve a race of filaria, by natural selection, which had learned to regulate the birth of its short-lived embryos so that there should be a maximum concentration of them during the hours when the necessary mosquito bites? Although this seems logical, it is nevertheless hard to believe that the embryos live so short a time, in view of the demonstrated long life of some non-periodic filariæ.

Within a few hours the blood ingested by a mosquito becomes a sticky mass in the insect's stomach, and holds fast the sheaths of any microfilariæ present, so that the latter easily slip out of them, like a foot out of a mired boot. Thus liberated, the ineffective squirming of the sheathed embryos changes to an effective snake-like progression of the naked worms. They move to the wall of the stomach, penetrate it, and migrate into the breast muscles within 24 hours; here they come to rest lying lengthwise between the muscle fibers (Fig. 158). The first evidence of development is a shortening of the body to about half its original length, and a thickening to double or more what it was. The embryos thus change from slender, graceful snake-like animals to sausage-shaped creatures (Fig. 157*A*). Meanwhile the digestive tract differentiates. The worms now grow both in length and girth, until they eventually reach a length of about 1.5 mm., with a diameter of 20 to 30 μ (Fig. 157*B*); this requires from ten or twelve days to several weeks. The larvæ now become active again, leave the thoracic muscles, and make their way down into the proboscis (Fig. 158), in the interior of the labium, although some get lost and end up in the palpi, legs, or elsewhere. When the mosquito bites a warm-blooded animal the larvæ emerge through the thin membrane between the labella and shaft of the labium, and creep out on the skin of the host, and penetrate it near the mosquito bite. It is only in warm, moist weather that this can happen successfully, for warmth stimulates the larvæ to activity, and moisture keeps them from drying up before they can effect an entrance.

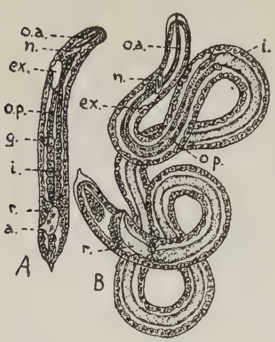

FIG. 157. Stages in development of *W. bancrofti* in mosquito. *A*, "sausage" stage; *B*, nearly mature larva; *a*, anus; *ex.*, beginning of "excretory" system; *g.*, genital rudiment; *i.*, intestine; *n.*, nerve ring; *o.a.*, thin anterior portion of esophagus; *o.p.*, thick posterior portion of esophagus; *r.*, rectum. (Adapted from Looss.)

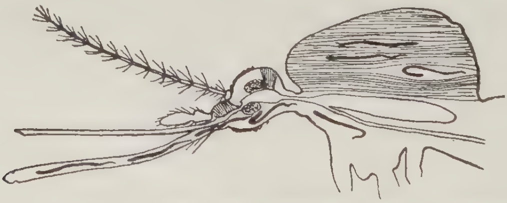

FIG. 158. Mature larvæ of *Wuchereria bancrofti* in thoracic muscles and proboscis of mosquito. (After Castellani and Chalmers.)

Nothing is known of the course pursued by the larvæ after they enter the skin, and very little as to the time required for sexual maturity to be reached. The large heart filaria of the dog, *Dirofilaria immitis*, matures 9 months after infection, and it is unlikely that the human filaria takes longer. The fact that children seldom show microfilariæ in their blood under five years of age, and Europeans only after many years of residence in an infected locality, is due either to the scantiness of the embryos in the blood, or to failure of the males and females to meet each other in the same glands or lymph ducts. There is little information about the length of life of the adults but evidence from other species suggests that they live at least four or five years. After death the adults become calcified.

Pathology. — Strangely enough, microfilariæ appear to do very little injury to the host, even when very abundant. The adults, on the other hand, are associated with a formidable list of diseased conditions due to interference with the normal functioning of the lymphatic system. It is nevertheless true that a very high percentage of people infected with *W. bancrofti* never show any ill effects at all; there are localities where the presence of the parasite was unsuspected until night blood examinations revealed the microfilariæ in a high percentage of the adults. In other localities, however, *e.g.*, the Ellice and Fiji Ids., a high percentage of the inhabitants show "filarial symptoms." At Mayotte, in the Comorro Ids., 59% of the grown men are reported to suffer from elephantiasis of the scrotum, and 80% with "filarial disease" of one kind or another; from $\frac{1}{3}$ to $\frac{1}{2}$ are incapable of reproduction. Symptoms of filarial infection seldom appear before 12 or 15 years' residence in an endemic area; the probable explanation is that it takes a number of years for any considerable collection of worms to be acquired and reach maturity, and a number more before they die. The frequency with which filarial diseases occur in the absence of microfilariæ in the blood may be due in part to the fact that dead adults are perhaps more likely to cause blockades of the lymphatic vessels than living ones, and a certain amount of immunity to subsequent infection may be acquired as the result of earlier infections, but it is also due in many instances to the inability of the microfilariæ to pass the dammed up lymph stream and get into the blood. In such cases they may be abundant in chylous urine or lymph drainages.

The blocking of lymph channels commonly results in enlarged lymph glands, and in varicose lymph ducts and thickened lymph trunks. Often the lymph is diverted into the scrotum, which enlarges and contains tense lymphatic swellings which, when ruptured, discharge large quantities of lymph or chyle; in other cases it is diverted to the bladder and is discharged with the urine, a condition known as chyluria; in other cases it is directed into the testes, tunica vaginalis, or joints.

One of the commonest manifestations of the infection is elephantiasis, which is a swelling, sometimes to incredible size, of various parts of the body, to which the lymph or chyle is diverted, so that they have the proportions of parts of elephants rather than of human beings (Fig. 159). The legs of one or both sides are most frequently affected, then the scrotum, and less commonly the arms, vulva, mammary glands, or parts of the head and neck. The disease commences with repeated attacks of painful swelling of the parts, accompanied by a fever; a condition known as lymphangitis. The tissues, infiltrated with lymph, do not quite resume their original size when the attack subsides, and there is a growth of connective tissue. With each recurring attack, at intervals of two or three weeks to several months, the affected part grows larger, till finally it reaches a tremendous bulk. Often the feet

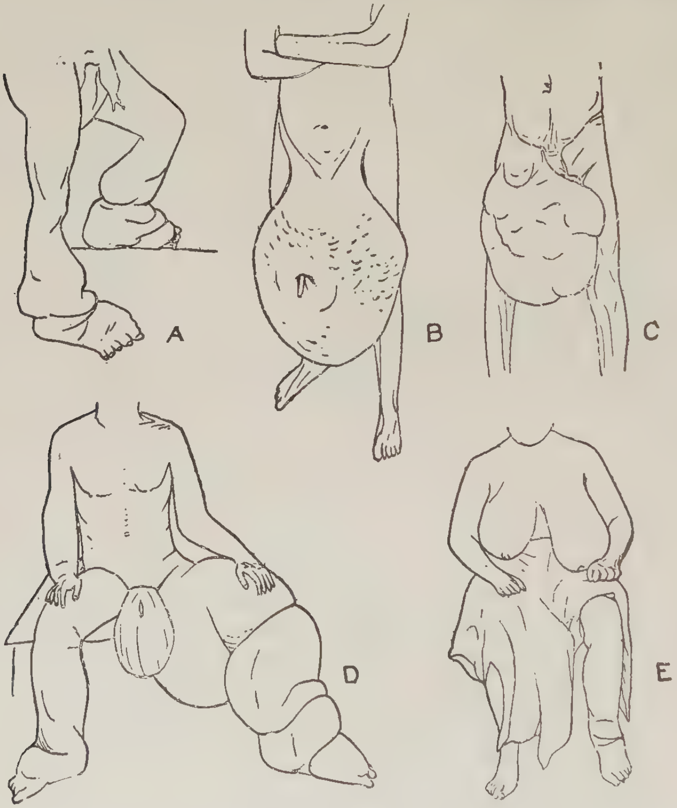

Fig. 159. A few extreme cases of elephantiasis; *A*, of legs and feet; *B*, of scrotum; *C*, varicose groin gland; *D*, of scrotum and legs; *E*, of mammary glands. (*A* and *B* sketched from photos from Castellani and Chalmers; *C*, *D* and *E* from Manson.)

or legs are so enlarged that it is impossible to lift them, and there is one case recorded of a scrotum weighing 224 pounds.

It is believed by many that filarial symptoms are usually due to secondary invasion of the injured lymph glands or ducts by bacteria. Filarial abscesses, filarial and elephantoid fever, etc., are almost certainly due to secondary infections with streptococci or staphylococci, and there is some evidence that the recurring attacks of lymphangitis, which ultimately result in disfiguring elephantiasis, do not occur in the absence of these bacterial infections.

Treatment and Prevention. — Although most of the drugs in the pharmacopeia have been tried in the hope of finding something that would be specific against filarial worms, no one has had any luck yet. Enlarged glands or ducts, or elephantoid growths, have to be treated symptomatically, by elevating the affected parts, by lymph drainage, or by surgical interference, for drug treatment is of no avail. Some workers have reported much improvement after vaccine treatment with cocci recovered from affected parts.

Control, of course, consists in avoiding infected mosquitoes in endemic areas, and, so far as possible, keeping persons with microfilariæ in their blood away from mosquitoes. This is especially difficult in the South Seas where *Aëdes variegatus* is present, but it has not so far proved feasible in any part of the tropics. Fortunately filariasis does not spread except in the presence of a considerable number of infected human beings in one locality, together with abundant mosquitoes. Infected negroes must have been brought to all parts of our Southern States, and *Culex quinquefasciatus* is everywhere present, yet the infection has become endemic only in Charleston, South Carolina. This must be due to the chance location there of a colony of negroes, large numbers of whom had microfilariæ in their blood. Although infected cases from Charleston go to all parts of the United States, no new focus of infection has been established. If, however, several dozens of individuals moved elsewhere and remained in a closely localized area, and opportunities were present for numerous *Culex* to bite them, it is entirely likely that the disease would be successfully transplanted. On the other hand, if all the infected individuals in Charleston were scattered, even to various parts of that city, it is reasonable to believe that the infection would die out.

The African Eye Worm, *Loa loa*

This worm, first discovered in Africans in the West Indies, is now known to be a common parasite in West and Central Africa from Senegal to Angola. The adults live in the subcutaneous tissue of man, and make excursions from place to place under the skin, causing itching and a " creeping " sensation; they show a special preference for creeping in and about the eyes (Fig. 161), and are very responsive to warmth. In a person sitting before a fire the worms become very active and move to exposed parts; they have been observed to travel at the rate of about an inch in two minutes.

The adult worms resemble pieces of surgical cat-gut, the females about 2 to $2\frac{1}{2}$ inches long and the males about $1\frac{1}{2}$ inches. The general anatomy is not unlike that of *W. bancrofti*, but the cuticle is provided with numerous little dew-drop-like warts along the lateral lines (Fig. 160). They produce sheathed embryos in the same manner as *W. bancrofti*, depositing them in the channels they make under the skin, whence they are carried by the lymph, presumably, into the blood stream. These embryos have a periodicity just opposite to that of *bancrofti* embryos, and swarm in the blood in the daytime, disappearing at night. The living microfilariæ of the two species are difficult to distinguish, but on stained slides they are readily distinguished by staining reactions and by minute details of structure (see p. 349).

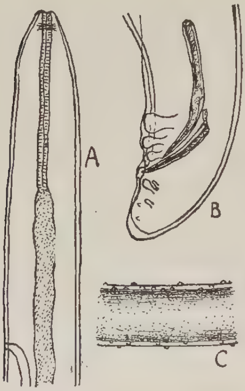

FIG. 160. *Loa loa.* *A*, anterior end, showing muscular and glandular parts of esophagus, and position of vulva, × 20; *B*, tail of male, showing spicules, ala, and papillæ, × 100. *C*, portion of body showing dew-drop-like warts on the cuticle along the lateral lines. (*A*, after Yorke and Maplestone; *B*, after Vogel; *C*, after Fulleborn.)

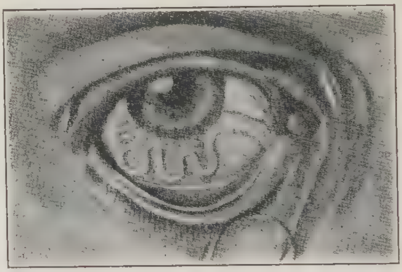

FIG. 161. *Loa loa* in eye. (After Fulleborn.)

The intermediate hosts are certain species of *Chrysops* (*C. dimidiata*, *C. silacea*, and possibly others), known as mango flies (see p. 530). This was long ago suspected by Manson on epidemiological grounds, but experimental evidence was first obtained in 1912–13 by Leiper and confirmed by Kleine (1915). The Connals in 1922 worked out the details; they remark that the African natives were already aware of the relation between mango flies and the eye worm. Most of the embryos ingested by a *Chrysops*, after escaping from their sheaths and penetrating the stomach wall, proceed to the muscles and fatty tissues of the abdomen, where hundreds may develop in a single fly. They are bent on themselves as they thicken and have sharp-pointed tails. Later they grow to a length of about 2 mm. and acquire a rounded tail with three little points, and in 10 to 12 days make their way to the proboscis, in which they collect as do *bancrofti* larvæ. When the fly bites, dozens of them may file out of the proboscis and quickly penetrate the skin.

The loa worm, in addition to the annoyance caused by its creeping under the skin, especially in and about the eyes, usually does very little harm. The worms seem especially active in their youth, and later sometimes retire to deeper parts of the body. In the eye they are painful, and the extraction has to be done expeditiously, before the disturbed worm flees to hiding places deeper in the body. Elliott describes a method of slipping a thread behind the worm and then tying it to keep it from getting away. It is a prevalent belief that loa infections in some way are responsible for the occurrence of painless edematous swellings, called "Calabar swellings," which are commonly about the size of pigeon eggs. They appear suddenly, last a few days, and then disappear, to reappear later somewhere else. The geographical distribution of the affection, together with the frequent proof of the presence of loa worms or their embryos, strongly suggest the complicity of the worm. The suggestion that the swellings are caused by emissions of embryos into the skin has been disproved, and no satisfactory explanation for them has been brought forth.

Acanthocheilonema perstans

This species of filaria is widely distributed in West and Central Africa, and also in northern South America and northern Argentina; it is limited to heavily forested, swampy regions in warm, moist climates. In some localities in Uganda and the Cameroons over 90% of the population harbor the microfilariæ in their blood. The adult worms are about as long as *W. bancrofti* but only about half as thick. They are found in connective tissue in the body cavities and pericardium. The microfilariæ are much smaller than those of *bancrofti* and *loa*, being about 200 μ in length and only about 4 μ in diameter, and they have blunt tails. They have no sheaths, and make no distinction between day and night. The infection seems to produce no evident symptoms, at least in the majority of cases, but Enzer has observed cases of persistant headache and drowsiness in individuals whose blood was teeming with the embryos, and in whom there was no other evident cause for the symptoms. Sharp (1928) has shown that the intermediate hosts in the Cameroons are minute nocturnal midges, *Culicoides austeni* and *C. grahami* (see p. 518). The larvæ develop in the breast muscles and emerge from the proboscis and head of the insect while it is biting. Sharp found about 7% of *C. austeni* naturally infected in a heavily infected locality in the Cameroons. The insects bite only in darkness, and protection is obtained by sleeping in the presence of even a very feeble light.

Mansonella ozzardi

This worm, related to *A. perstans*, is common in parts of the West Indies and neighboring coasts of South America, and it is probable that a microfilaria which occurs in 25 to 30% of the natives of northern Argentina, and described as *Filaria tucumana*, belongs to this species. The adult females are about 3 to 4 inches long and one-fourth mm. or less in diameter; they are characterized by a pair of flap-like processes, with fleshy cores, at either side of the tail (Fig. 162*B*). Only a single incomplete male has ever been found. The adults were obtained from connective tissues in the abdominal cavity. The microfilariæ are much like those of *A. perstans*, — small, unsheathed, and non-periodic, but differ in having pointed tails without nuclei. There is no evidence that the worm is pathogenic. The intermediate host is unknown; development, but only to the "sausage" stage, occurs in certain mosquitoes. It is not unlikely that a *Culicoides* will be found to be the transmitter.

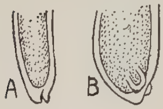

FIG. 162. Tails of females of *Acanthocheilonema perstans*, (*A*), and *Mansonella ozzardi* (*B*). Note split tail of former, without fleshy cores in the flaps, and the lappets of the latter, with fleshy cores. (After Leiper.)

Onchocerca

The genus *Onchocerca* contains two species of filariæ which occur in man, and a number of others in domestic animals. Some of the latter, especially *O. gibsoni*, cause hard fibrous nodules or " worm nests " in the muscles and subcutaneous tissue of the briskets and flanks of Australian cattle, resulting in financial losses amounting to millions of dollars. One human species, *O. volvulus*, is widely distributed in west and central Africa while the other, *O. cæcutiens*, is found in Guatemala and neighboring parts of Mexico. A probable case has been observed in French Guiana also.

The Onchocercas are very long, semi-transparent, thread-like worms, the females reaching a length of 10 to 20 inches with a diameter of less than half a millimeter, while the males are only about $1\frac{1}{2}$ inches long and 0.2 mm. thick. They are at once recognizable by hoop-like thickenings of the cuticle which run spirally around the body like the coils of a cylindrical spring (Fig. 163). The worms lie, usually one female and several males, in tangles in the interior of hard nodules in subcutaneous tissue which vary from the size of a pea to that of a pigeon's egg; these nodules are formed by fibrous capsules which the host forms around the parasites (Fig. 164). The nodules usually contain numerous microfilariæ also. In some localities, both in Africa and Guatemala, practically every adult and a high percentage of the children are infected. The African and American worms, though indistinguishable morphologically, differ markedly in their biology and pathologic effects. The African *O. volvulus* nodules are especially common about the bones and joints, particularly over the knee, elbow and hip joints, over the ribs and on other parts of the trunk, but very rarely on the scalp. Fulleborn points out that while each species of *Onchocerca* seems to have a special predilection for certain parts of the body, it is possible that the frequency of *O. volvulus* nodules over bones may be due to tissue reactions here which do not occur in other places, and unencapsuled worms may be more frequent than is suspected. *O. volvulus,* though extremely common in natives in some localities, practically never attacks Europeans. The American *O. cæcutiens*, on the other hand, lives in nodules practically always if not exclusively on the head and scalp, especially about the ears, and is very common among white plantation managers as well as natives. This species, though apparently harmless in some cases, is described by Robles (1919) as producing painful swellings of

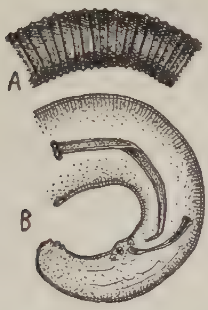

Fig. 163. *Onchocerca volvulus; A*, portion of body showing spiral thickening; *B*, tail of male, showing spicules and papillæ. (Adapted from Fulleborn.)

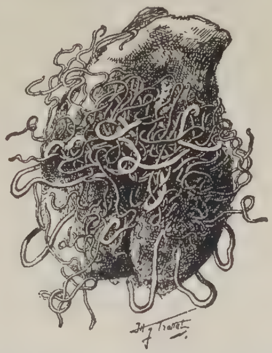

Fig. 164. An opened *Onchocerca* tumor showing tangled worms inside; × 2. (After Brumpt.)

parts of the head, accompanied by fever, known as "coastal erysipelas." Another peculiar effect of the infection, without parallel in parasitology, is a serious interference with vision, resulting in dim and indistinct sight or in complete blindness. The cornea becomes opaque and the pupil contracted. Within a few hours after the worm nodules are removed the sight is improved, and may become normal in a couple of days. The suggestion that the eye disturbance is due to toxins produced by the worms has no experimental proof. Innumerable microfilariæ are left in the skin, and perhaps also in the eyes, after the nodules are removed, so the prompt return to normal is so far inexplicable.

The uteri of the females are packed with coiled embryos enclosed in thin shells, usually with polar extensions; Fulleborn (1929) describes them as resembling oranges wrapped in tissue paper, the paper being twisted at the ends. The embryos leave the eggs, as a rule, after they have been deposited in the nodules; they escape readily from the prisons which enclose their parents and make their way, not into the blood stream, but into the connective tissue just under the skin, where they accumulate in large numbers. Sometimes they emerge by hundreds when a bit of excised skin is placed in a saline solution for two or three hours. These microfilariæ have no sheaths, they have sharply pointed tails, and they vary in size from about 200 to 350 μ in length and from 5 to 9 μ in diameter.

The intermediate host in Africa was shown by Blacklock (1926) to be a species of blackfly, *Simulium damnosum* (see p. 524). When this tiny pest bites, it spends a minute or more rasping a minute ragged hole in the skin, thus apparently dislodging and stimulating to activity any larvæ present in the adjacent parts of the skin. A tsetse fly, imbibing many times the quantity of blood taken by a blackfly, only occasionally takes up a few embryos as it drives its proboscis through infected skin, but over 80% of the fed blackflies become infected, and some take 100 to 200 embryos in a single meal. The embryos become very active in the stomach, penetrate its wall, and go to the thoracic muscles. Here they go through the usual "sausage" stage and then grow into elongate larvæ, about 0.75 mm. in length and about 20 μ in diameter. These migrate into the head and proboscis, whence they emerge as do the larvæ of other filariæ, when the insects bite. The whole development requires a week or more, according to temperature.

There has been considerable dispute as to the injuriousness of Onchocerca infections. In most cases *O. volvulus* seems to produce no ill effects, and the nodules are seldom painful or disturbing. On the other hand some authors believe that the worm can cause elephantiasis and disturbances of the lymphatic system, and others think that various skin diseases are caused by the larvæ in the skin. A skin disease known as craw-craw in West Africa is thought by some to be caused by these larvæ; the skin is covered with an eruption of little vesicles or papules, sometimes resembling scabies. Although the Onchocerca embryos are commonly present, it is now known that they are also abundant in apparently normal skin. The peculiar effects produced by *O. cœcutiens* in Guatemala have already been mentioned.

There is no treatment other than excision of the nodules, which is usually easy. Prevention consists in avoiding the haunts of black-flies during the daylight hours when they bite, and the clearing of brush around houses and villages to keep them away.

Other Filariæ

There are on record scattered cases of a number of other adult filariæ, and several common microfilariæ, which are of doubtful nature or unknown affinities. One adult, known as *Filaria conjunctivæ*, has been found occasionally in cyst-like tumors of the eye, nose, arm and mesentery in Europe and India. The females are 6 to 8 inches long and 0.5 mm. broad, while the males measure a little over 2 inches. This worm causes a burning or itching sensation and localized edema. There are a few records of several other forms, most of them sexually immature, from the eye socket, lens, skin or other places, none of which have been definitely classified, and all of which are probably only accidental human parasites. There is one record, from Brazil, of a filaria from the heart, *Dirofilaria magalhãesi*, a worm closely related to the common heart filaria of the dog.

Several species of microfilariæ of unknown parentage have been discovered. *Mf. malayi* (see p. 349) is a sheathed form, smaller than *bancrofti*, found abundantly in the Malay archipelago, and possibly also in India. In the endemic regions no filarial symptoms occur except elephantiasis. These microfilariæ are nocturnal, but do not develop in *Culex quinquefasciatus. Mf. streptocerca* (see p. 350) is an unsheathed form much like the embryo of *perstans*, but longer. Like the embryos of *O. volvulus* it does not occur in the blood, but only in the skin, choosing the skin of the arms and back. Unlike the embryos of Onchocerca, however, these microfilariæ are rarely ingested by *Simulium damnosum*, and they were never seen to be ingested by *Culicoides*. No development takes place in *Simulium*.

The Guinea-worm, *Dracunculus medinensis*

This huge worm, somewhat more distantly related to the typical filariæ than those hitherto discussed, is a common and important parasite in parts of Asia and Africa; it has also been introduced and established in some localities in tropical America. The "fiery serpents" which molested the Israelites by the Red Sea, and were mentioned by Moses, were probably guinea-worms. It is now, as in ancient times, one of the scourges of life in Western Asia from Central India to Arabia, as well as in Egypt and much of Central Africa.

The adult female worm lives in the deeper layers of the subcutaneous tissue where, often, she can be more readily felt than seen, except when she produces a skin lesion through which she gives birth to myriads of wriggling young. She reaches a length of from $2\frac{1}{2}$ to 4 feet, usually about 3 feet, with a diameter of from 1 to $1\frac{1}{2}$ mm., thus resembling a long piece of cord. Often she can be seen lying, like a small varicose vein, in loose coils just under the surface of the skin. The head end is bluntly rounded while the tail is attenuated and sharply hooked. The males are practically unknown, but there is evidence that they are relatively mere midgets, an inch to an inch and a half in length.

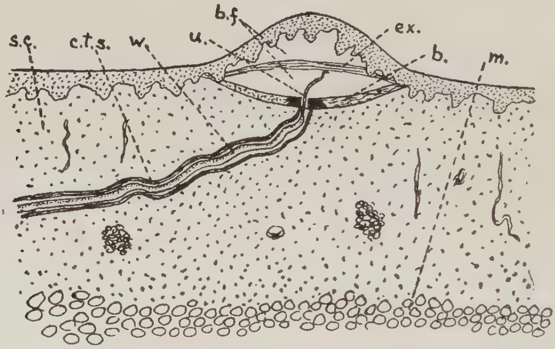

FIG. 165. Diagram of guinea-worm in the skin at the time of blister formation; *b.*, base of ulcer, *b.f.*, blister fluid; *c.t.s.*, connective tissue sheath of worm; *ex.*, layer of exudate; *m.*, muscle layer; *s.c.*, subcutaneous tissue; *u.*, extruded uterus of worm; *w.*, worm. (Adapted from Fairley.)

When ready to bring forth her young, the guinea-worm is instinctively attracted to the skin, especially to such parts as are likely to, or frequently do, come in contact with cold water, such as the arms of women who wash clothes at a river's brink, or the legs and backs of water-carriers. The worm pierces the lower layers of the skin with the front end of her body and excretes a toxic substance which irritates the tissues and causes a blister to form over the injured spot (Fig. 165). The blister eventually breaks, revealing a shallow ulcer, about as large as a dime, with a tiny hole in the center. When the ulcer is douched with water a milky fluid is exuded directly from the hole or from a very delicate, transparent projected structure which is a portion of the worm's uterus. This fluid is found to contain hordes of tiny coiled larvæ with characteristic straight projecting tails. The larvæ (Fig. 166) are from 0.60 to 0.75 mm. in length. An hour or so later a new washing with cold water will bring forth a fresh ejection of larvæ and so on until the supply is exhausted, a little more of the uterus being extruded each time. After each ejection of the larvæ the protruded portion of the uterus dries up, thus sealing in the unborn larvæ. This process can be looked upon only as a wonderful adaptation for the preservation of the race. As we shall presently see, the tiny larvæ utilize various species of *Cyclops* (Fig. 167), small freshwater crustaceans, as intermediate hosts. If the larvæ were not deposited in water, or if they were all poured at once into any bit of water with which the skin of the host came in contact, the chance of their reaching a suitable *Cyclops* would be very small. The result would usually be family suicide and eventually race suicide. The repeated birth of a limited number of progeny each time the skin of the host comes in contact with water is therefore a successful solution to a problem which to a blind, burrowing, unmeditative worm must otherwise present insuperable difficulties. When all her young have been deposited, under the stimulus of contact with water, the parent worm shrivels and dies and is soon absorbed by the tissues on which she formerly preyed and through which she roamed.

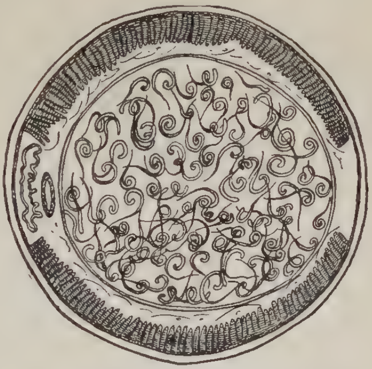

Fig. 166. Cross section of guinea-worm showing uterus filled with embryos. × about 30. (After Leuckart.)

The embryo worms, safely deposited in water, unroll themselves and begin to swim about in a fashion peculiar to themselves. Their bodies are somewhat flattened and they have a slender tail. They swim by a few quick sculling motions of the tail, followed by a pause, then a few more strokes, etc., in the manner of a tadpole. In turbid water they remain alive for several days but eventually perish unless they come in contact with a *Cyclops*, into the body of which they make their way.

They usually enter by way of the mouth, sometimes as many as six or ten entering a single *Cyclops*. In a day or two they leave the stomach of *Cyclops* and enter the body cavity. In spite of the relatively large size of the worms the crustaceans seem to feel very little inconvenience, and seldom succumb even to very heavy infection.

The young guinea-worms become fully developed in *Cyclops* in from 12 days to several weeks, according to the temperature, meanwhile having undergone one and perhaps two moults. They are then about one mm. in length, and ready to infect a new host. Entrance to the new host is probably accomplished by the accidental drinking of a *Cyclops* with unfiltered water. The female worms become adult in their new host in about a year, so the larvæ can again be deposited at about the time that *Cyclops* becomes abundant.

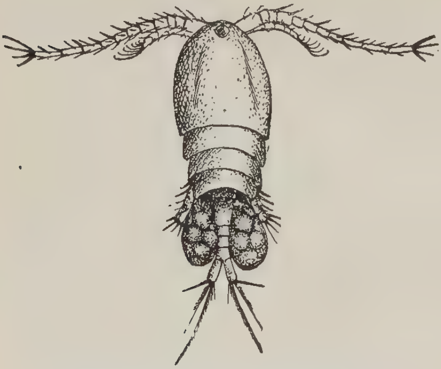

Fig. 167. A Cyclops, some species of which serve as intermediate hosts of guinea-worms. × about 25.

There is abundant epidemiological evidence as to the method of infection. In western India the infection is always associated with "step-wells," which, instead of being provided with buckets and ropes, are approached by steps, the people standing foot or knee-deep in the water while filling containers. During this time the parent worm ejects her offspring, and at the same time previously infected Cyclops are withdrawn with the water. In African villages ponds function in a similar manner.

Pathology. — The worms, which parasitize a very high percentage of people in localities where the conditions for its spread are favorable, are of profound importance to these people. In some places about 25% of the inhabitants are incapacitated for about a month each year.

The first symptoms appear simultaneously with the beginning of the blister formation, and consist of urticaria, nausea and vomiting, diarrhea, asthma, giddiness, and fainting; some or all of these symptoms may be present. Fairley (1925) believes they are due to absorption of the toxin employed by the worm to form the blister. The nature of the symptoms strongly suggests an anaphylactic reaction, but goats injected with guinea-worm extracts show similar symptoms. Injection of adrenalin brings about very rapid improvement.

Later symptoms result from secondary invasion of the ulcer by bacteria. The worms are usually mechanically extracted and, being elastic, are likely to break. The broken end of the worm draws back, carrying with it into its connective tissue sheath various bacteria which produce abscesses. These may cause such severe infection as to necessitate amputation, or may even lead to fatal blood poisoning. If the worm is located near a joint, the latter may be involved and lead to permanent deformities. These occur with deplorable frequency in villages of the " Deccan " in India.

When the worms have successfully fulfilled their mission in life by evacuating all their embryos, and have not been extracted, they die and are soon absorbed, but when a worm dies before establishing communication through the skin to the outside world it often becomes calcified, and may be in evidence for many years.

Treatment of guinea-worm infection by means of drugs is of little or no avail. Fairley quotes an Indian proverb which expresses the true state of affairs — " One guinea-worm but a thousand remedies." Drugs given by mouth are a complete failure, and in spite of occasional enthusiastic reports of success with injection of such drugs as salvarsan and tartar emetic, this method of treatment has also failed. Natives often apply various applications locally after the ulcer has formed, but usually succeed only in causing secondary infections.

Extraction of the worm by winding it out on a stick is a time-honored method which, with a few scientific refinements, is still the only beneficial mode of attack. Native medicine men extract the worms by this method through the ulcer by repeatedly douching the head of the worm with water and then winding it out a little at a time, or, having located the worm in the skin, by cutting out a small disk of skin with an improvised razor until the worm is exposed. When a loop of the worm has been obtained it is pulled out by continuous or intermittent traction. If fortunate enough to get out the whole worm without breaking it, green powder made of neem leaves, together with a choice assortment of contaminating bacteria, is applied to the wound, and the unfortunate patient is turned loose to fight his battle with the bacteria instead of the relatively innocent worm. If he loses his leg or his life it is the will of the Gods, and no fault of the doctor. Another native method is to apply a cone-shaped piece of metal over the exposed part of the worm and suck it vigorously until a negative pressure is created sufficient to draw the tissue up into the cylinder. The tongue is then applied and the finger quickly substituted and after a few minutes the worm may be found in the tube.

By the use of local anesthetics and aseptic precautions, the mechanical extraction method, using an incision to hook out as long a loop of the worm as possible, cutting this off, and then extracting the posterior end through a second incision and the anterior end through the ulcer, if present, followed by aseptic excision of the ulcer, proves very successful, and complete healing usually follows in less than a week, as contrasted with the usual month. Injections of antiseptics into or in the vicinity of the worm has not met with general success.

Prevention of the infection would be extremely simple if it were not for the scruples of the natives, often of religious nature, as to where and how they obtain and use their water. In India wherever step-wells are replaced by other types which keep the legs or arms out of the water, guinea-worm disappears, but to interfere with wells which have been in use for centuries and are hallowed by religious or traditional incidents, is no easy matter. If the water were strained through muslin to remove *Cyclops*, guinea-worm would disappear, but even this is difficult of accomplishment. However, education and governmental pressure eventually bring results, and many areas in India which have suffered from guinea-worm for centuries have been freed in recent years by altering the wells. No practical means of killing *Cyclops* in water, and keeping them out, has been discovered.

Spiruroid Worms

The superfamily Spiruroidea contains a very large number of worms which are parasitic in all kinds of vertebrates. They occur principally in insect-eating hosts, since infection usually if not always results from the ingestion of infected insects or other invertebrates. For this reason man is not a normal host for any of these worms, though he is an occasional host for a number of them.

Gongylonema. — The members of this genus are very slender filaria-like worms which live in the walls of the esophagus or mouth cavity. There is much difference of opinion as to how many distinct species there are; they occur in all kinds of herbivorous domestic animals, as well as in pigs, bears, rodents, monkeys and man. Most helminthologists consider the forms found in man to be *G. pulchrum*, but Stiles prefers a non-committal name, *G. hominis*, for the human parasites. There are seven human cases recorded, five of them from white women in southern United States and two from Italy, all of them immature worms. The patients were all aware of the active migrations of the worms under the lips or cheeks and were much annoyed by them; they move so rapidly that considerable dexterity is required to remove them. Two of the patients also had nervous disorders which disappeared after they got rid of their parasites.

The female worms, less than a half-millimeter in diameter, reach a length of about six inches, and the males a little over 2 inches, but they are often much shorter. The head end of the worm is embellished with about eight rows of wart-like bosses, which is a very distinctive character. The males are provided with caudal alæ, and with one very long and one very short spicule; the females have the vulva situated a little in front of the anus. They produce thick-shelled eggs containing embryos which develop after the eggs are eaten by cockroaches, dung beetles, and perhaps other insects, in the body cavity of which the larvæ coiled in thin cysts can often be found. When such infected insects are eaten by the final host, infection results. Obviously human infection could not be common since the human appetite tends in other directions.

Considerable interest was created in these worms a few years ago by Sambon's theory that they, or other worms migrating in the tissues, were a common cause of human cancer. Sambon even collected data purporting to show an epidemiological relationship between cancer and an abundance of roaches. The most important basis for this view was that certain species of *Gongylonema* inhabiting the stomach wall of rodents have actually been shown to be, in some way, the cause of stomach cancers in their hosts. There is no evidence that the Gongylonemas of larger animals, however, have such an effect.

Physoloptera. — This genus contains relatively large stout worms at first sight resembling small Ascarids. They have a pair of lips provided with teeth on the inside, enclosed in a cuticular collarette. The males have caudal alæ which meet in front of the anus and are almost bursa-like in appearance. A very large number of species have been described, from all kinds of terrestrial vertebrates, living in the stomach or intestine. The human Physalopteras have been described as two species; *P. caucasica*, found once in the Caucasus, and *P. mordens*, quite common in natives of tropical Africa; Faust considers these as a single species, *P. caucasica.* In Africa monkeys seem to be the reservoir hosts. The females are from 1 to 4 inches long and from 1.2 to 2.8 mm. in breadth, while the males are about half this size. Nothing is known about the clinical effects of this species, but the writer has observed severe irritation and erosion of the stomach wall of cats infected with Physalopteras in India. The females deposit unstained eggs with thick, smooth shells, containing embryos. The life cycle of none of the eighty-odd species of this genus is known, but an insect almost certainly serves as an intermediate host.

Thelazia callipæda. — This slender little worm, possible more nearly related to the filariæ than to the spiruroids, inhabits the conjunctival sac of the eye of dogs, and occasionally man, in India, Burma and China.

Occasionally the worms creep out over the eye ball but sooner or later return to their nest in the corner of the eye. The worms are from 7 to 17 mm. long, the males somewhat smaller than the females. The cuticle is pleated into well-defined striations with sharp edges. There are no lips, but there is a small buccal vestibule. The vulva is anterior in position and the male has no caudal alæ.

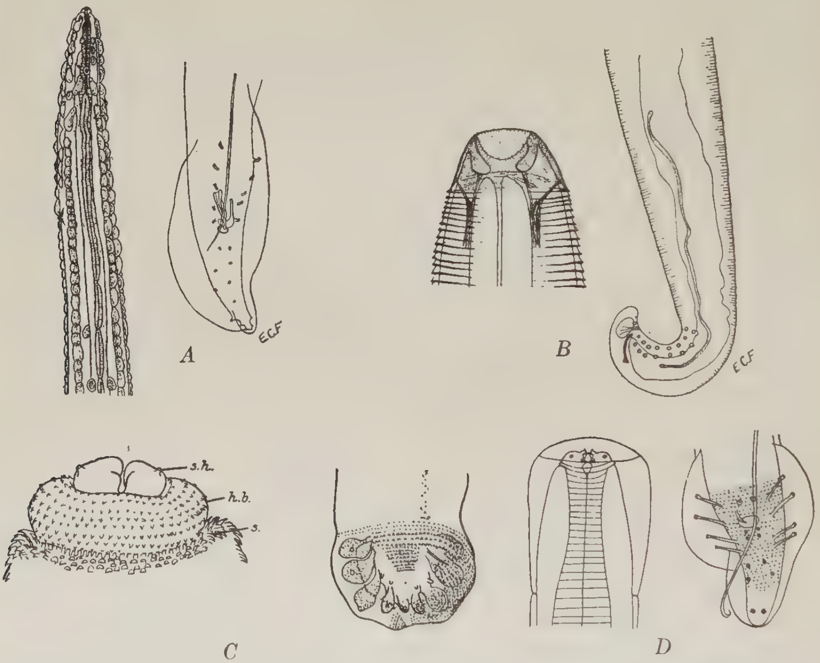

Fig. 168. Heads and tails of male Spiruroid worms found in man. A. *Gongylonema pulchrum;* head, × 45, (after Ward); tail, × 48, (after Faust). B. *Thelazia callipæda;* head, × 210; tail, × 33, (after Faust). C. *Gnathostoma spinigerum;* head and tail, × 39, (after Baylis and Lane). D. *Physaloptera caucasica;* head, × 22, (after Leiper); tail, × 16, (adapted from V. Linstow). (A, B and D from "Human Helminthology" by Ernest Carroll Faust, Ph.D., Lea and Febiger, Publishers, Philadelphia; C from "Nematode Parasites of Vertebrates" by Yorke and Maplestone, J. and A. Churchill, Publishers, London.)

The females deposit embryonated eggs with transparent shell membranes which soon swell, and from which the worms push out a finger-like extension, leaving a balloon-like portion of the membrane attached at their tail ends. The larvæ in this condition resist desiccation for several days. It is probable that further development takes place in an insect intermediate host, but experiments done by Faust with a number of theoretically possible insects were negative, as were attempts to transmit the worms directly.

The movements of the worms in the eye cause considerable irritation and a general nervous reaction, with a copious flow of tears. At first the eye is not seriously affected, but Faust (1928) observes that in the course of time the repeated scratching of the surface of the eye ball by the serrated cuticle of the worm causes the formation of scar tissue, and the eye gradually develops a cloudiness, progressing outward from the worm nest, which ultimately reduces the vision of an infected dog. Only a few human cases, all from China, have been recorded.

Gnathostoma spinigerum. — This is a very robust worm, quite unlike most of the Spirurata. It has a globular swelling at the head end which is armed with eight or more rows of thorn-like hooks. At the anterior end of this spiny head is the mouth, bounded by a pair of fleshy lateral lips. Behind the swollen head the body is clothed with overlapping rows of toothed scales, which gradually dwindle away posteriorly.

The natural hosts of this worm are wild and domestic cats and rarely dogs. In tigers the females may reach a length of over two inches but in cats they are usually somewhat less than an inch in length, and about 2 mm. in diameter. The adults inhabit large, hard tumors, sometimes an inch in diameter, in the stomach wall of their hosts; these open by one or more pores into the stomach and are inhabited by from one to a half-dozen worms. They are known to cause fatal peritonitis when they open into the body cavity, and the seasonal occurrence of the parasites in cats, as seen by the writer in Calcutta, suggests that they may be invariably fatal, for it seems impossible that the tumors could disappear completely soon after the worms had left. The eggs of the worm, which have a characteristic plug at one pole, like the glass stopper of a bottle, do not contain embryos when deposited; they enter the stomach and are voided with the feces.

The life cycle is obscure. The writer discovered that almost every snake in the vicinity of Calcutta was infested with encysted larval gnathostomes, sometimes by hundreds, differing from those in cats in having only four rows of spines on the head. When these are fed to cats they emerge from the cysts, burrow through the wall of the digestive tract into the body cavity, and then enter principally the mesenteries and liver, causing much destruction as they burrow in the tissues. The writer also found many cats naturally infected with these larvæ in the liver, and found one cat which showed some of the parasites having transformed to a stage with 8 rows of spines but still sexually immature, in process of entering the stomach wall from the peritoneal side. Now, cats do not commonly indulge in a diet of snakes, nor do snakes usually partake of cats or cat's feces as food, so it is probable that the infection is side-tracked in the snakes. Very likely an insect or mollusc is the intermediate host; when this is eaten by a snake the larvæ re-encyst in the mesenteries, but when eaten by a cat they develop first in the liver and subsequently in the stomach wall.

Human infection with immature worms of this species, either wandering in the skin or in skin abscesses, have been recorded in a number of instances. As in the case of many other parasites in a strange host, these worms, in the presumable absence of the usual guides on which they depend to reach their normal habitat, get lost and end up in places where they do not belong, and where, probably, they cannot mature. Altogether 8 cases of immature subcutaneous gnathostomes have been recorded in man, all in southeastern Asia. The writer found eggs of the worm in presumably human feces on two occasions in Burma, so it seems likely that the worm sometimes finds its way to the proper destination in the human host. In view of the dangerousness of the infection in cats, human infection is a thing to be greatly feared. Snake-eating, as practiced by some of the wilder tribes of southeast Asia, is extremely dangerous.

There is also a single record of a case of human infection with another species of *Gnathostoma*, *G. hispidum*, normally found in pigs in the Old World. This worm, too, was hopelessly lost, wandering aimlessly under the skin.

The Giant Kidney Worm (*Dioctophyme renale*)

This giant nematode, the largest one known, lives normally in the pelvis of the kidney of dogs and wild carnivores, and more rarely in the body cavity, but it has also been recorded from the pig, horse, ox and man. As noted on p. 348, its relationships are very uncertain. It is a cylindrical, blood-red creature; the female reaches a length of 8 to 40 inches with a diameter of 5 to 12 mm., while the males are about half this size. The lipless mouth is surrounded by papillæ. In both sexes the anal opening is terminal, the cloaca of the male being surrounded by a bell-shaped, muscular cup without rays. The thick-shelled, brown eggs are pitted except at the poles, and it takes up to six months for the embryos to develop in them, but the eggs remain alive for five years or more. The whole life cycle is not known, but Ciurea (1921) claims to have infected a puppy by feeding raw fish (*Idus idus*) containing encysted larvæ.

The worms cause severe injury to the kidneys, eventually destroying them completely; both renal and nervous symptoms occur in infected dogs. According to Brumpt there are 9 cases of human infection on record.

CHAPTER XIX

LEECHES

The annelids as a group are not of such primary importance as parasites as are the two other great groups of " worms." In fact only one class, the Hirudinea or leeches, contain species which are parasitic on the higher animals.

No boy who has ever experienced the unbounded delights of hanging his clothes on a hickory limb and immersing his naked body in a muddy-bottomed river or pond is unfamiliar with leeches or " bloodsuckers." Still more familiar with them is any tourist who has journeyed on foot through the jungles of Ceylon or Sumatra, or any explorer who has walked through the warm moist valleys of the Himalayas or Andes, and who has been attacked by hordes of bloodthirsty land-leeches which infest these places. Nor is it likely that the thirsty traveler in North Africa or Palestine who stops to gulp a few mouthfuls of water from a pool or stream, and who accidentally imbibes one of the leeches which infest such waters, will not always remember the bleeding and unpleasant sensations, and perhaps dangerous symptoms, which follow the settlement of the leech in the mouth or nasal passages.

General Anatomy. — The leeches are segmented worms belonging to the phylum Annelida, in company with earthworms, kelpworms, etc. They are distinguished from other annelids by the absence of any bristle-like outgrowths from the body (setæ) and by the presence of two suckers, one at the mouth for sucking food, and a large one at the posterior end for adhering to surfaces. The rings of the body as seen on the surface do not correspond to true segments of the body as they do in other annelids; there are several rings to most of the segments. The bodies of leeches are extremely elastic, and can be stretched at will to several times the contracted length. In fact the usual method of locomotion, other than an undulating mode of swimming, is by alternately expanding and contracting the body, adhering first by the large posterior sucker, then by the smaller oral sucker, and so forth.

Nearly all leeches feed exclusively on blood. The digestive tract (Fig. 64, p. 200) is peculiar in that the esophagus is supplied with a series of " crops " or side pockets in which blood can be stored up as a reserve supply to be gradually drawn back into the stomach and intestine and digested as needed. Since some leeches can fill up with three times their own weight in blood, and can live on this supply for a year or more, meals are few and far between. The saliva of the leech has the power of preventing the coagulation of blood, and therefore blood continues to flow for some time after the leech has "got his fill" and let go. Like other annelids, leeches have a true blood system and a series of nephridia, little coiled tubes, a pair in each segment, which function as primitive kidneys. There are no special gills or other respiratory organs; oxygen is absorbed directly through the skin which is constantly kept moist.

Leeches are hermaphroditic, *i.e.*, both sexes are represented in the same individual, but the egg of one leech is always fertilized by a sperm from another. In most leeches the eggs are deposited in a stiff mucous cocoon which is secreted by a portion of the body. When the eggs are laid the cocoon is slipped over the head like a jersey, the ends closing together to form a capsule. After a little manipulation with the oral sucker the mother leech imbeds the cocoon in moist soil, near the edge of water in the case of aquatic species.

Importance as Parasites. — The ordinary pond and river leeches which adhere to bathers are of little or no economic importance as human parasites. Of these the well-known medicinal leeches, *Hirudo*, used for sucking out infections or bad blood, are the best known examples. They are furnished with powerful suckers and sharp-pointed pincer-like jaws, and can therefore easily penetrate the skin and suck blood from any part of the surface of the body. They can usually be persuaded to release their hold when removed from water.

With the weak-jawed members of the genera *Limnatis* and *Hæmopis*, commonly known as horse leeches, it is quite different. These animals seek to penetrate the natural openings of the body and fasten themselves to the mucous membranes, especially in the mouth and nasal cavities, where they may cause such extensive bleeding as to bring about the death of the host. Of perhaps even greater importance, because more difficult to avoid, are the bloodthirsty land-leeches which have already been mentioned as infesting many tropical countries. Leeches serve as intermediate hosts for many species of trypanosomes of fishes and other aquatic animals, and it is not impossible that they may be found to transmit some species to man.

Leeches in the Mouth or Nose. — The leeches which habitually settle themselves in the mouth or nasal cavities of men or animals are inhabitants of muddy-bottomed ponds, ditches, reservoirs, troughs, etc., and enter the mouth or nose of their host while he is drinking. According to Masterman, leeches of the species *Limnatis nilotica* become so abundant in northern Palestine in late summer and autumn that almost every horse and mule passing through these parts has a bleeding mouth. The Nile leech, *Limnatis nilotica*, is the most plentiful species around the shores of the Mediterranean, but leeches of the genus *Hæmopis*, with similar habits, also occur over a large part of Europe. Troublesome aquatic leeches have been reported by travelers in the lake regions of central Africa also, and in some other warm countries, especially Formosa.

The young leeches, which are usually the ones which enter the mouth or nose during drinking, are only a fraction of an inch in length, but the adults reach a length of several inches. The average length of *Limnatis nilotica* is about one inch or less.

A person while drinking from infected pools, especially in dusk or at night, is very likely to suck in one or more of these leeches. During the process of swallowing the parasites attach themselves to the walls of the mouth or pharynx and may migrate into the nose or larynx. Seldom, if ever, are the leeches completely swallowed, and even if they should reach the stomach they would probably be killed at once and digested. It is a peculiar and indeed unfortunate fact that, while the leeches which attack the surface of the body fill with blood and then let go, those which settle on the mucous membranes keep their hold for days or weeks, though they shift their positions, leaving the old bites to continue bleeding. As already stated, the loss of blood from the wounds made by the leeches is often sufficient to cause an extreme or even fatal anemia, though the hemorrhages of clear blood are never great in quantity at any one time. The blood flows out of the nose or into the throat or trachea, in the latter cases being constantly coughed up. Masterman describes the case of a man in Palestine, attacked by leeches, who for nearly a week had been " spitting blood " and had a spittoon full of practically pure blood by his side, every few minutes adding more. His lips were blue, and he was unable to speak above a whisper. Every few minutes he had a short cough. Often when the leech is attached in the larynx beside the vocal cords, the body flops back and forth during breathing, and has been known to cause asphyxiation by blocking the trachea. Cases are on record where leeches, having fallen into one of the bronchi, have died and disintegrated, and thus caused destructive bacterial infections to set in. The presence of leeches in the mucous membranes is often accompanied by severe headaches. Sometimes leeches which have settled in the nose have the revolting habit of protruding themselves from the nostrils and allowing a portion of the body to wander over the upper lip. They are, however, so elusive that they can be captured only with great difficulty.

The treatment employed for leech infestations of the nose or mouth varies greatly in different countries. According to Masterman the natives of Palestine transfix the leech, if within reach, with a thorn from a native tree, and muleteers extract leeches from mules' mouths with packing needles. When the parasite is beyond reach of this transfixing process these people smear some of the thick deposit which collects in their tobacco pipes on a splinter of wood and endeavor to touch the leech with it; this is said to cause the leech to lose its hold. Masterman found the most successful means of removing a leech to be either to seize it with suitable forceps, or to paralyze it with cocaine. Much difficulty is often experienced in seizing the writhing, slippery creature with a pair of forceps even when it can be seen clearly with a mouth mirror, partly on account of the spasmodic contractions of the larynx and the frequent coughing. Usually strong salt solution causes them to release their holds, but if this is not successful they can be paralyzed and disengaged by touching them with cocaine solution on a swab. To avoid the possibility of the leech falling into the trachea the patient is made to lie on a couch with his head hanging over the edge.

Land-leeches. — Of perhaps greater importance, because far less easy to avoid, are the attacks of the land-leeches of many tropical countries. These leeches are found in Ceylon, Japan, Sumatra, Philippine and East Indian Islands, Australia, and the humid mountain meadows of the Andes and of the tea gardens in the Himalayas. Sir J. Emerson Tennent in his book on " The Natural History of Ceylon " writes as follows: " Of all the plagues which beset the traveler in the higher grounds of Ceylon the most detested are the land-leeches, *Hæmadipsa ceylonica.* They are not frequent in the plains, which are too hot and dry for them, but among the rank vegetation of the lower hill country, which is kept damp by frequent showers, they are found in tormenting profusion. They are terrestrial, never visiting ponds or streams. In size they are about an inch in length and as fine as a common knitting needle, but they are capable of distension till they equal a quill in thickness and attain a length of nearly two inches. Their structure is so flexible that they can insinuate themselves through the meshes of the finest stocking, not only seizing on the feet or ankles, but ascending to the back or throat, and fastening on the tenderest parts of the body. In order to exclude them the coffee planters who live among these pests are obliged to envelope their legs in " leech garters " made of closely woven cloth. The natives smear their bodies with oil, tobacco ashes or lemon juice, the last serving not only to stop the flow of blood, but also to expedite the healing of the wounds. In moving, the land-leeches have the power of planting one extremity on the earth and raising the other perpendicularly to watch for their victim. Such is their vigilance and instinct that, on the approach of a passerby to a spot which they infest, they may be seen amongst the grass and fallen leaves on the edge of a native path, poised erect, and prepared for their attack on man and horse. Their size is so insignificant and the wound they make is so skillfully punctured that both are generally imperceptible, and the first intimation of their onslaught is the trickling of the blood or a chill feeling of the leech when it begins to hang heavily on the skin from being distended with its repast. Horses are driven wild by them and stamp the ground in fury to shake them from their fetlocks, to which they hang in bloody tassels. The bare legs of the palankin bearers and coolies are a favorite resort, and as their hands are too much engaged to pull them off the leeches hang like bunches of grapes round the ankles. Both Marshall and Davy mention that during the march of troops in the mountains when the Kandyans were in rebellion in 1818, the soldiers, and especially the Madras Sepoys, with the pioneers and coolies, suffered so severely from this cause that numbers perished.

"One circumstance regarding these land-leeches is remarkable and unexplained: they are helpless without moisture, and in the hills where they abound at all other times they entirely disappear during long droughts; yet reappear instantly at the very first fall of rain, and in spots previously parched, where not one was visible an hour before, a single shower is sufficient to reproduce them in thousands. Whence do they reappear! May they, like rotifers, be dried up and preserved for an indefinite period, resuming their vital activity on the mere recurrence of moisture?"

Similar reports come from travelers in other tropical countries. Alfred Wallace encountered land-leeches in Sumatra where he found them infesting the leaves and herbage by the side of the paths through the forests. At the approach of a traveler as indicated by footsteps or a rustling of leaves, the leeches stretched themselves out at full length and attached themselves to any part of the passerby which they happened to touch. Their presence and the loss of blood was seldom felt during the excitement of walking, but a dozen or so had to be picked off every evening. Dean C. Worcester in his book on the Philippines says "the moist earth swarmed with leeches

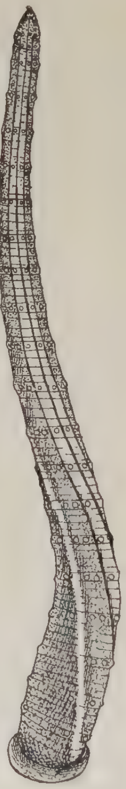

FIG. 169. Japanese land-leech, *Hæmadipsa japonica*, extended. × 2. (After Whitman.)

which crawled through my stockings and bit my ankles until my shoes were soaked with blood." One species, *H. japonica* (Fig. 169), is common in parts of Japan. The land-leech of Australia belongs to a different genus, *Philæmon.*

In any of the localities infested by land-leeches it is advisable to bind the feet and legs in leech-proof cloth, this being preferable to various ointments which are supposed to discourage the leeches from their meal. In a tropical climate where so many diseases and unfavorable conditions beset one on every side, it is important to take every precaution to keep in perfect health. The loss of blood from the attacks of leeches, and the portal given for entrance of bacteria and other organisms in the wounds made by them, might make all the difference between life and death in the struggle for existence in these disease-plagued climes.

PART III — ARTHROPODS

CHAPTER XX

INTRODUCTION TO ARTHROPODS

To the average person it is astonishing to learn that the insects and their allies, constituting the phylum Arthropoda, include probably more than four times as many species as all other animals combined. It is even more startling for egotistical humanity to realize that this is not the age of man, but the age of insects, and that man is only beginning to dispute with insects first place in the procession of animal life in the world. In the vast horde of animal forms which constitute the Arthropod phylum are included some species which are distinctly valuable to the human race, such as bees, the silkworm, the thousands of insects (Diptera and Hymenoptera) parasitically destructive to injurious species and the predaceous beetles; a great number which are indifferent as regards their economic importance serving, perhaps, only to arouse admiration for their beauties or disgust for their loathsomeness; and many which are of great importance as crop pests or as annoyers of domestic stock or of man himself. Only relatively very few, a mere handful, are injurious to man as parasites or as disease carriers, but these few are of almost incalculable importance. As mere parasites the parasitic arthropods are of minor importance, but it is in their capacity as intermediate hosts of other parasites or as mechanical carriers of disease germs that these animals have to be reckoned with as among the foremost of human foes. Every arthropod, parasitic or otherwise, which habitually comes in direct or indirect contact with man must be looked upon as a possible disease carrier. The rôle of arthropods in the dissemination of disease is a matter about which practically nothing was known 35 or 40 years ago. A French physician, Dr. Beauperthuy, in 1853 was one of the first to express a belief in the dissemination of various diseases by mosquitoes and in the rôle of the housefly in the spread of pathogenic organisms. In 1879 Manson first proved insects to be intermediate hosts of human parasites, in the case of *Filaria* and the mosquito. Since that time many of the most important human diseases have been shown not only to be transmitted by arthropods but to be *exclusively* transmitted by certain species or genera. In the latter category, as far as we know at present, are malaria, by some physicians rated as the most important human disease; yellow fever, which formerly haunted South and Central America, and still lurks in parts of those places and in its home in West Africa; relapsing fever, present in almost every part of the world, ready to break forth into devastating epidemics whenever conditions permit; typhus fever, a dreaded dragon of death which hovers over every war camp in the world; trench fever, which was the cause of more morbidity among the allied soldiers during the Great War than all other factors combined; Rocky Mountain spotted fever, which has rendered practically uninhabitable some of the richest valleys in northwestern United States, and allied diseases transmitted by mites in Japan and the East Indies (tsutsugamushi or flood fever) and by ticks in India and Africa; dengue and pappataci fever, which sweep over cities and countries, affecting a high proportion of the total population; Oroya fever of the Peruvian Andes; sleeping sickness, one of the blackest clouds hanging over " Darkest " Africa; Chagas' disease, one of the many plagues of tropical South America; bubonic plague, which once destroyed one-fourth the population of Europe and caused over ten million deaths in India in the 25 years 1898–1923; filariasis, a disease which in some localities causes malformations in a high percentage of the inhabitants; guinea-worm infections; lung fluke infection; some tapeworm infections; and some others of less importance. In all probability there will be added to this formidable list kala-azar, not the least important of the many scourges of mankind in Bengal and Assam, and some other parts of the world.

There are many other diseases which, although they may be transmitted in other ways also, and in most instances usually are, are nevertheless transmitted by insects to various extents. Most of the diseases listed in the preceding paragraph, except plague, are caused by worms or protozoa, or organisms believed to be protozoan in nature, or by spirochætes or what are at present known as filterable viruses. The diseases caused by the ordinary bacteria are usually transmitted by such agencies as contagion, water, milk, vegetables, dust, etc., but may be mechanically transmitted by insects, *e.g.*, typhoid, dysentery, tuberculosis, leprosy, etc. It is evident that any insect may serve as a disseminator of disease in this mechanical way in proportion to the degree to which the structure of its body facilitates the carrying of germs, and to the extent that it associates with man or his food, and that its habits bring it in contact with disease germs. In some instances the insects not only disseminate the disease by simple contamination, but also serve as " culture tubes " in which the organisms multiply. Such is the case with plague, which, in its bubonic form, has no other practical method of distribution than by insects, although the pneumonic type is transmitted like pneumonia. In tularemia, also, the germs multiply in the gut of insects, and in nature are normally transmitted by them, but human infections more commonly result from handling of diseased animals. Anthrax also multiplies in the digestive tract of certain insects.

Relationships. — The insects and their allies, constituting the phylum Arthropoda, are the most highly organized of invertebrate animals, and stand at the head of their particular line of evolution. They find their nearest allies in the segmented worms or annelids, *i.e.*, earthworms, leeches, etc., but most of them show a great advance over their lowly cousins. Like the annelids they have a segmented type of body, though in some types, such as the mites, all the segments become secondarily confluent. Like the annelids, also, the arthropods are protected by an external skeleton which usually consists of a series of horny rings encircling the body. The most obvious distinguishing characteristic of the arthropods is the presence of jointed appendages in the form of legs, mouthparts and antennæ. Internally they are distinguished from other invertebrates in that the body cavity, so conspicuous in the annelids, has been entirely usurped by a great expansion and running together of blood-vessels, so that in the place of the usual body cavity or celome there is a large blood-filled space. Within this space are blood-vessels and a so-called heart, which retained their individuality while the other vessels fused. These vessels are not, however, closed, but open into the general blood space at each end.

Classification. — The phylum Arthropoda is divided by Comstock into thirteen classes. One of these, the Onychophora, includes a small group of animals, until recently included in the single genus *Peripatus*, which is very primitive and helps to bridge the gap between the arthropods and the annelids. *Peripatus* is a free-living, worm-like animal, and of no interest here. There are two classes of aquatic arthropods, breathing by means of gills, one of which is almost entirely extinct except the modern horse-shoe crab, whereas the other, the Crustacea, is of some concern to us as intermediate hosts of some parasitic worms. The class Arachnida, considered an offshoot of the aquatic series, include some parasites and some disease transmitters. There are three classes of degenerate forms of doubtful position, one of which, the Pentastomida, interests us, since its members are all parasites and some of them attack man. The remaining six classes include air-breathing and primarily terrestrial animals. Five of the classes include worm-like, wingless forms, such as the centipedes and millipedes, which are sometimes grouped together into a single class Myriapoda; they do not concern us as parasites or disease vectors. The remaining class, the Hexapoda or true insects, represent the climax of the arthropod evolutionary series, and accounts for the vast majority of the existing arthropods. Of the thirteen classes, then, only four concern us as human parasites or disease transmitters, namely, the Crustacea, the Arachnida, the Pentastomida, and the Hexapoda.

The Crustacea, including crayfish, water fleas, etc., are primarily arthropods of the water. They are geologically of great antiquity and among them are the most primitive of the typical arthropods. Their appendages are usually numerous and, taking the group as a whole, show a wonderful range of modifications for nearly every possible function. Crustaceans breathe by gills. Although many are parasites of aquatic animals, none can be considered as parasites of man or other land animals. Three cases are known in which Crustacea serve as the intermediate hosts of human parasites, namely certain species of *Cyclops* as hosts for the guinea-worm (see p. 365), certain species of *Cyclops* and related copepods as hosts for tapeworms of the genus *Diphyllobothrium* (see p. 266), and crabs and crayfish as the second intermediate hosts of the lung fluke (see p. 236).

The Arachnida, including spiders, scorpions, mites, etc., are for the most part highly developed arthropods, representing the terminus of a separate line of evolution. They probably had a common origin with the Crustacea, but have become adapted to terrestrial life. The members of this class have four pairs of legs as adults, two pairs of mouthparts and no antennæ. The head and thorax, which usually form distinct sections of the body in insects, are grown together forming a cephalothorax, and in the ticks and many mites not even the abdomen remains as a distinct section. They breathe by means of invaginations of the body which contain gills arranged like the leaves of a book, whence the name " book lungs." Some of the higher arachnids also have a system of branched air tubes or tracheæ in the body similar to those found in the insects and myriapods. Only one of the eight orders of Arachnida, namely the Acarina (mites and ticks), contain parasitic species, and many of these are important disease vectors. The Pentastomida are degenerate worm-like creatures which in the adult stage have no appendages except two pairs of hooks near the mouth. If it were not for the larval forms, which have two pairs of short legs, their affinities with the arthropods might be doubted. They were formerly included, for want of a better way of disposing of them, with the mites, but it seems preferable, for the present at least, to dignify them to the extent of placing them in a class by themselves. They are excellent examples of the " degenerating " effect of parasitic life. They have no circulatory or respiratory organs. Like many of the parasitic worms, these animals, in some cases at least, have intermediate hosts in which they undergo their larval development.

The Hexapoda, or insects, represent the zenith of invertebrate life. They are terrestrial arthropods which breathe by tracheæ. Their appendages, however, are reduced to one pair of antennæ, three pairs of mouthparts (one pair more or less fused together) and three pairs of legs with usually the addition, if not secondarily lost, of two pairs of wings. The wings are really mere outgrowths or folds of the integument or "skin" of the insect, between the two layers of which are branches of the tracheæ, represented by the "veins" in the wings of adult insects. There is a fundamental plan of arrangement of the veins which is variously modified in different insects, but absolutely fixed in any given species. The venation of the wings is often of great value in the identification of genera or species of insects. An insect is always readily divisible into three parts, the head, thorax and abdomen. The head, in addition to the antennæ already mentioned, generally bears two compound eyes sometimes of relatively enormous size, usually several simple eyes or ocelli, and the mouthparts.

The Cuticle. — In the absence of any internal supporting skeleton in insects, the rigidity of the body is maintained by a cuticle more or less reinforced with a horny substance known as chitin. Since the chitin is unaffected by caustic soda or potash, and since the characters used in the identification of insects are largely cuticular, it is often useful to boil insects in caustic solutions to remove all the fleshy parts, and leave the chitinous parts in a more readily examinable condition. When first formed the cuticle is thin and flexible, and is later thickened and hardened by secretion of chitin by the underlying living cells. The chitinization is not continuous over the whole body, otherwise the insect would

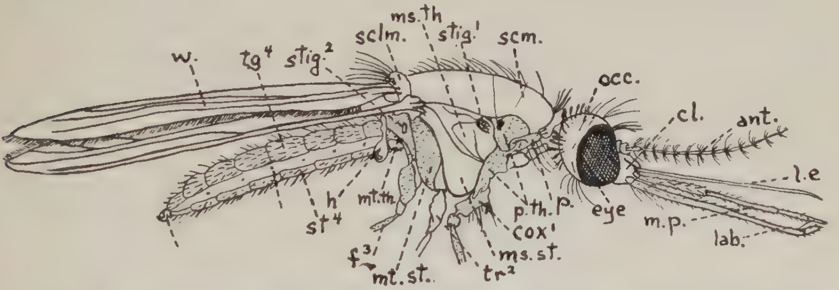

FIG. 170. Diagram of mosquito showing parts of body. The prothorax and metathorax, with their respective legs, are dotted, the mesothorax not dotted; *ant.*, antenna; *cl.*, clypeus; *cox*,[1] coxa of first leg; *eye*, eye; *f*[3], femur of third leg; *lab.*, labium; *l.e.*, labrum-epipharynx; *m.p.*, maxillary palpus; *ms.st.*, mesosternum; *ms.th.*, mesothorax; *mt.st.*, metasternum; *mt.th.*, metathorax; *p.*, patagium; *p.th.*, prothorax; *occ.*, occiput; *sclm.*, scutellum; *scm.*, scutum; *st.*[4], sternite of fourth abdominal segment; *stig.*[1] and [2], first and second stigmata; *tg.*[4], tergite of fourth abdominal segment; *tr.*[2], trochanter of second leg; *w.*, wing. (After Nuttall and Shipley, from Hindle.)

find itself imprisoned and immovable in its case; instead the chitin is laid down in plates or rings, allowing movement and expansion of the parts of the body. Usually the parts of the head are entirely enclosed in chitin except the movable appendages, and the thorax likewise, but some or all of the segments which make up the abdomen remain distinct and movable, with non-chitinized areas between them. Even in each segment the chitin does not form complete rings; in the abdomen each segment has a dorsal plate or tergite and a ventral one or sternite; in the thorax at least some of the segments show a pair of lateral divisions also, the pleurites. Each single chitinized plate is called a sclerite, and the lines of separation between them are the sutures.

The surface of the cuticle may bear a variety of projections, some fixed and others, the cuticular appendages, connected by joints. Of the former there are usually numerous conical or wart like nodules, and also fixed spines and hairs. Of the appendages the most important are the setæ or bristles, or hairs. They are hollow out-growths from single cells imbedded in the epidermis. The setæ may be bristle-like, spine-like, plumose, or scale-like, and may serve to clothe the body, to act as ducts of glands, or to function as sense organs. Their form and arrangement are often of great value in classification, and the study of them has been dignified by the term " chætotaxy."

As arthropods grow they gradually become too large for their cuticles. The living cells of the epidermis then lay down a new, thin, elastic cuticle under the old one. Certain cells produce a sort of "moulting fluid" which partially dissolves the old cuticle making it easier to shed after a split has been formed in it. After the moult the new cuticle hardens, and then gradually thickens again by formation of more chitin.

Mouthparts of Insects. — Incredible as it may seem at first thought, the mouthparts of all kinds of insects, from the simple chewing organs of a grasshopper to the highly modified piercing and sucking organs of biting flies and mosquitoes and the great coiled sucking tube of butterflies and moths, are modifications of a single fundamental type. This type is represented in its simplest form in the chewing or biting type, as found in grasshoppers and beetles (Fig. 171). The mouthparts in these insects consist of (1) an upper lip or labrum (Fig. 171, *Lbr.*); (2) a lower lip or labium (Fig. 171, *Lbm.*), really formed of a pair of organs fused together, each bearing a segmented appendage, the labial palpus (Fig. 171, *Lab. p.*); (3) a pair of hard, horny, toothed mandibles or jaws (Fig. 171, *Mand.*) lying just under the lower lip, which chew up food by a horizontal instead of vertical movement; (4) a pair of maxillæ (Fig. 171, *Max.*), lying between the mandibles and lower lip, each bearing a segmented appendage more or less like those on the lower lip, and called the maxillary palpus (Fig. 171, *Max. p.*) and (5) the hypopharynx (Fig. 171, *Hyp.*), a short fleshy organ lying in the midst of the other organs, and comparable in both form and function with the tongue of vertebrate animals. In addition to these parts there is a horny lining of the upper lip and roof of the mouth cavity known as the epipharynx. This structure is usually closely associated with the upper lip, so that the combined organ is spoken of as the "labrum-epipharynx."

The extent of the modifications which these mouthparts may undergo is wonderful, especially in insects where they are modified for sucking or piercing. In the true bugs the mandibles and maxillæ are prolonged into needle-like organs, the maxillæ often armed with sawlike teeth at their tips, and the lower lip is developed into a thick, fleshy, jointed proboscis, grooved on its upper side to form a sheath for the piercing organs (Fig. 208). The labrum is a short movable flap, and the hypopharynx is very slightly developed. In the Diptera, which include the mosquitoes, gnats, blackflies, tsetse flies and other biting flies as well as houseflies and blowflies, there are several different types of modifications. In mosquitoes the mouthparts (Fig. 276) are much as in bugs, but the labrum-epipharynx and hypopharynx are also modified into long piercing

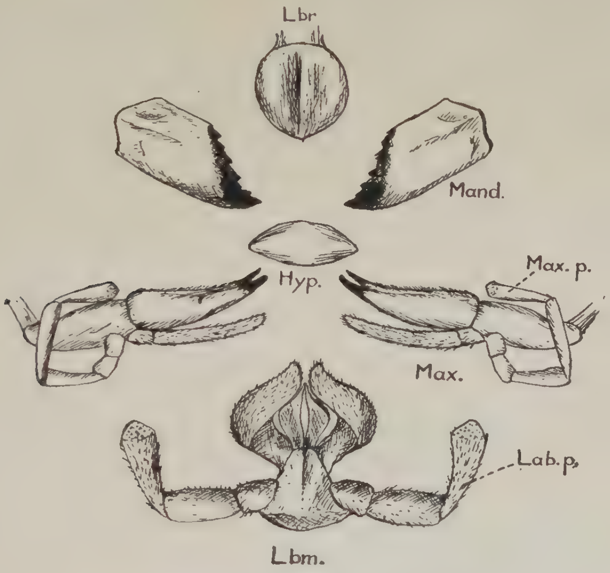

FIG. 171. Simple mouthparts of a chewing insect (*Stenopalmatus*); *lbr.*, labrum, or upper lip; *mand.*, mandible; *hyp.*, hypopharynx or tongue; *max.*, maxilla; *max. p.*, maxillary palpus; *lbm.*, labium or lower lip (really a second pair of maxillæ fused together); *lab.p.*, labial palpus.

organs, and the latter is fashioned into a true hypodermic needle for injecting salivary secretions. In blackflies and tabanids (Figs. 248 and 254) the parts are similar but the piercing organs are shorter and more bladelike, resembling daggers rather than needles. In the tsetse flies and stable-flies (Figs. 259 and 270) the lower lip itself is the chief piercing organ, the labrum-epipharynx and hypopharynx contained in it being needle-like and capable of forming a sucking tube by apposition with each other. The mandibles and maxillæ are much reduced or rudimentary, but the maxillary palpi are conspicuous, and in tsetse flies form a perfect sheath for the proboscis. In the houseflies and their non-blood-sucking allies the mouthparts are most modified, being all molded together to form a fleshy proboscis especially fitted for lapping up liquid foods. In fleas the mouthparts (Fig. 224) are somewhat as they are in the biting flies, but the maxillæ are not modified as piercing organs but as pyramidal organs used for holding the flea in position while piercing and sucking, and the sheath for the piercing organs is formed from the labial palpi instead of from the labium or lower lip itself. The mouthparts of sucking lice (Fig. 217) are still not thoroughly understood but the piercing and sucking organs, whatever parts they really represent, can be retracted into a sheath under the pharynx. The mouthparts of such insects as moths, bees, wasps, etc., are also remarkable examples of structural adaptations, but they do not concern us here.

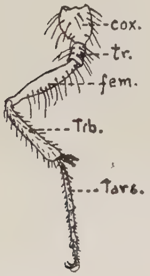

FIG. 172. Leg of an insect; *cox.*, coxa; *tr.*, trochanter; *fem.*, femur; *tib.*, tibia; *tars.*, tarsus. (After Comstock.)

Legs. — The legs of different classes of arthropods vary greatly in number of segments, and it is difficult to homologize the segments in one class with those in another.

In the Arachnida the legs typically have seven segments which, beginning next to the body, are named as follows: (1) coxa; (2) trochanter; (3) femur; (4) patella; (5) tibia; (6) metatarsus; and (7) tarsus. The tarsus may be composed of several segments, and is often terminated by one or more claws, and frequently a median sucker, caroncle, or other modification which either bears or lies between the claws.

In the insects the legs consist of five parts, the coxa, trochanter, femur, tibia and tarsus. The coxa articulates the leg with the body and sometimes appears more like a portion of the body than a segment of the leg. The trochanter is a very short inconspicuous segment between the femur and coxa, and sometimes appears like a portion of the femur. The femur and tibia are large segments. The tarsus, or foot, consists of a series of segments, most commonly five; often the first segment is much the longest. Usually the tarsus is terminated by a pair of claws, sometimes only one. In the sucking lice there is a single very large claw which acts with a projection of the tibia as a pincer-like structure. Often there are pad-like structures, pulvilli, which have glandular hairs or pores through which an adhesive substance is excreted, permitting the insects to walk on the under side of objects. Sometimes there is a pulvillus at the base of each claw and also a similar median structure between them, called an empodium.

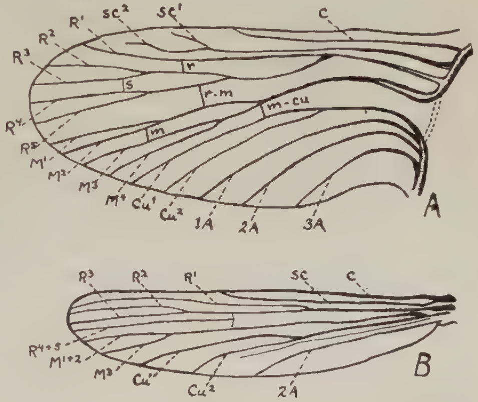

FIG. 173. *A*, diagram of the primitive tracheæ of an insect wing from which the veins are derived; *B*, venation of a mosquito's wing showing a comparatively simple modification; *C*, costa; $sc.^{1 \text{ and } 2}$, subcosta, first and second branches; $R^{1 \text{ to } 5}$, radius, first to fifth branches; $M^{1 \text{ to } 4}$, media, first to fourth branches; $Cu^{1 \text{ and } 2}$, cubitus, first and second branches; *1A*, *2A* and *3A*, first to third anal; *r*, radial cross-vein; *s.*, sectorial cross-vein; *r-m.*, radio-medial cross-vein; *m*, medial cross-vein; *m-cu.* medio-cubital cross-vein. (*A*, after Comstock; *B*, original.)

Wings and Venation.—The structure of the wings of insects is often of great use in classification and identification. Only in two primitive orders of non-parasitic insects are the wings primarily absent, although in many forms, especially parasitic ones, *e.g.*, lice and fleas, they are secondarily lost as modifications for the mode of life of these insects. Typically there are two wings, borne by the second and third segments of the thorax. The wings originate as sac-like folds of the body wall, but the upper and lower surfaces become applied to each other and thus appear as simple membranes. Where they flatten down against the tracheæ they become thickened, forming hollow supports or "veins." In most insects the majority of the veins are longitudinal but there are usually a few cross-veins, and in some kinds of insects these are very numerous. Figure 173*A* shows the hypothetical primitive arrangement of the venation of an insect wing; the venation of the wings of all insects can be traced to this primitive arrangement, but the modifications brought about by coalescence, anastomosis, atrophy, and addition of extra branches and cross-veins often makes it as bad as a Chinese puzzle to determine the true homologies of the resulting veins. The eight principal veins with their typical branches are shown in the figure. The spaces between the veins are called cells, and are named after the longitudinal veins behind which they occur. When a cell is divided by a cross-vein the more basal portion is named the first part, the more distal part the second. Figure 173*B* shows the wing of a mosquito as an example of a comparatively simple modification.

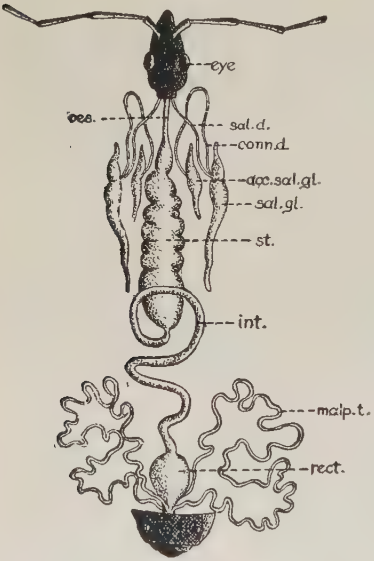

Fig. 174. Digestive tract of a Reduviid bug; *acc. sal. gl.*, accessory salivary gland; *conn. d.*, connecting duct between salivary glands; *int.*, intestine; *malp. t.*, malpighian tubules; *oes.*, esophagus; *rect.*, rectum; *sal. gl.*, salivary gland. (Partly after Dufour.)

General Anatomy. — The digestive tract of insects (Fig. 174) is often highly developed and differentiated. The blood-sucking insects have a muscular pharynx in the head which acts like a suction pump. In the bedbug, for instance, the powerful muscles which are used to expand the pharynx and thereby produce suction occupy a considerable portion of the inside of the head, and the area on top of the head to which they are attached is distinctly visible on the outside. The pair of salivary glands open into the floor of the pharynx, but they themselves are usually situated in the thorax. Often they are very highly developed. In the true bugs they have connected with them accessory salivary glands, which in some species may serve at least in part as storage vats for holding the secretion temporarily. In mosquitoes (Fig. 274) the salivary glands consist of three lobes, one lobe being noticeably different in appearance and secretion from the others. The pharynx connects with the stomach by a slender esophagus. Various means are used by blood-sucking insects to increase their capacity. In the bugs (Fig. 174) the stomach is extremely distensible and serves as a storage reservoir. In fleas and many biting flies there is an expansion of the esophagus anterior to the true stomach, called the proventriculus, in some insects provided with heavily chitinized tooth-like structures; in mosquitoes there are capacious pouch-like food reservoirs or outgrowths from the esophagus in addition to the proventriculus (Fig. 274). Just behind the true stomach at the beginning of the intestine there open a number of long slender tubes, the "Malpighian tubules" (Fig. 174, *malp. t.*). These are the excretory organs, corresponding to the kidneys of vertebrate animals.

Their function is to collect the waste matter of metabolism from the blood; in the tubules the soluble wastes are changed into insoluble substances, so that when emptied into the intestine, to be voided through the anus, they cannot be re-absorbed. The length of the intestine varies, being usually longer in vegetable-feeding insects than in carnivorous ones. It often has a marked expansion, the anal pouch, at its posterior end.

The tracheæ of insects, as already intimated, are really a ventilation system consisting of air tubes ramifying all through the body even to the tips of the antennæ and legs. They open by a series of pores along the sides of the insect known as spiracles, which function as do the nostrils of higher animals. The principle of oil sprays for insects is to form a film of oil over the spiracles, so that the insects will suffocate.

The nervous system of insects is very highly developed for invertebrate animals. In some species the instincts, especially those connected with providing for their offspring, simulate careful and accurate reasoning, and it is difficult not to fall into the error of looking upon them as animals endowed with a high degree of intelligence.

Most insects are well provided with sense organs. There are widely distributed sensory setæ which serve as organs of touch, like the whiskers of a cat. Especially abundant are sensory organs which serve as organs of taste or smell; an insect is not limited in the distribution of these organs as are mammals, for they can smell (or taste) with most of the surface of the body, the bases of the wings, the antennæ, and the legs. Much has been written about the acute olfactory sense of such animals as dogs and wild mammals but these animals are only crudely equipped as compared with insects, which can detect extremely dilute odors over distances of probably a mile or more. Insects appear to depend more on the sense of smell than on any other type of sense perception. The compound eyes of insects are the most highly specialized of any optical organs known, but are nevertheless not as efficient as the eyes of vertebrates; their power of accommodation is limited, and insects can see distinctly only for short distances, in most cases probably not more than a few yards. The image produced by the thousands of facets is a mosaic one, with no overlapping of the parts of the picture in eyes adapted to daylight, but with some overlapping in " night eyes." The latter consequently are capable of distinguishing objects and movements in very dim light, but do not give sharp images. Some simple eyes or ocelli are probably very efficient, while others are incapable of doing more than distinguishing between light and dark. Many insects, at least those producing sounds, have some organs of hearing, but in many instances they are hard to recognize as such. Certain grasshopper-like insects have ears on the legs, whereas the mosquitoes utilize the basal segment of the antennæ for this purpose. Larvæ have modified auditory organs in some of the abdominal segments.

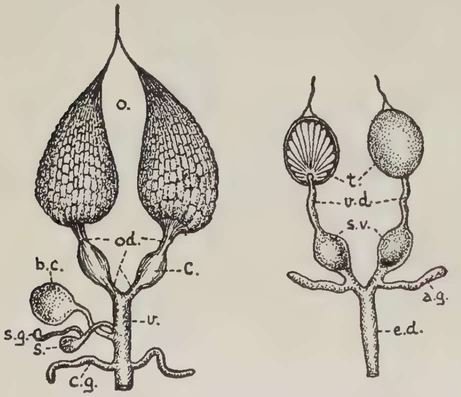

Fig. 175. Diagrams of female (left) and male (right) reproductive organs of an insect; *o.*, ovary, *od.*, oviducts; *c.*, egg-calyx; *b. c.*, copulatory bursa; *s. g.*, spermathecal gland; *s.*, spermatheca; *v.*, vagina; *c. g.*, collaterial gland; *t.*, testes; *v. d.*, vas deferens; *s. v.*, seminal vesicle; *a. g.*, accessory gland; *e. d.*, ejaculatory duct. (After Comstock.)

The reproductive organs consist of a pair of ovaries and oviducts in the females and of a pair of testes and sperm ducts in the males. Most insects have accessory reproductive organs in the form of glands and storage reservoirs for the seminal fluid both in the males and females. The external genital openings in both sexes are near the posterior end of the abdomen on the ventral side. The ovaries are usually compact, spindle-shaped bodies made up of a variable number of parallel "ovarian tubes," all opening into a common oviduct. The germ cells gradually develop into mature eggs as they pass down the tubes; in most insects there are also non-reproductive cells in the tubes which function as "nurse cells" for the nutrition of the eggs. In most insects the two oviducts unite into a common vagina. All female insects have a "spermatheca" or storage sac for sperms, since the pairing of the sexes occurs only once in insects, whereas the egg-laying period may extend over a long time. The eggs are fully formed, with shells, before being fertilized, but one or more minute pores, the micropyle, is left through which a sperm may enter, usually during the passage through the vagina. In some insects, especially the fleas, the shape of the spermatheca is one of the best identification characters in female specimens. In many insects there is a well-developed ovipositor which may simulate a miniature saw, borer, or piercing organ for depositing the eggs in the places characteristic of the species; this versatile organ may be, in the Hymenoptera, modified into a sting. The testes, like the ovaries, are made up of a group of tubules in which the sperms progressively develop. Each testis has a vas deferens which unites with its mate into an ejaculatory duct corresponding to the vagina of the female; its terminal portion may be chitinized and evaginated as an intromittent organ. Many male insects have highly developed external genitalia in the form of claspers and accessory parts fitted for holding the female at the time of pairing. In many instances, for example in mosquitoes and many other Diptera, the details of the structure of the external genitalia are of great value in identification of closely related species. Some species of Culex cannot certainly be differentiated in any other way. (See Figs. 239, 277.)

Life History. — Most insects hatch from eggs deposited by the mother, but in some instances living young are born; in the case of the tsetse flies the eggs not only hatch before birth but the young are retained in the body of the mother until they have reached the pupal stage. In this case only a few young are produced, but most insects lay large numbers of eggs, some all at once, some in batches at intervals, and others individually day after day. As regards life history, three different types can be recognized among insects. In the primitive subclass Apterygota alone there occurs " direct development " in which the newly hatched insect is nearly a miniature of its parent, and merely increases in size. The two common types of development are by incomplete and complete metamorphosis. Insects which have an incomplete metamorphosis are those which differ more or less from their parents when hatched, but which gradually assume the parental form with successive moults or sheddings of the skin. The young or " nymphs " of such insects invariably lack wings, and often have other characteristics different from their parents. In such insects as lice, in which the wings are absent in the adult, there is very little difference except in size between the young and adult forms. Insects which have a complete metamorphosis are those in which, as in the butterflies, the newly hatched insect is totally different from the parent, and does *not* gradually assume the parental form. The early stages of such insects, which are usually worm-like, are called " larvæ " in distinction from the " nymphs " of gradually transforming insects. Upon completion of their growth and development they go into a resting and more or less inactive stage, and are then known as pupæ. The pupa may have no special protection, as in the case of mosquitoes and midges; it may retain the last larval skin as a protecting case called the puparium, as in muscid flies; or it may be encased in a coccoon of silk thread spun by the larva as a protection from the hostile world before going into its mummy-like pupal state, as in the case of fleas and many moths. Although apparently inactive, the pupal stage is one of feverish activity from a physiological standpoint, for the entire body has to be practically made over. This transformation necessitates the degeneration of practically every organized structure in the body, and a re-formation of new organs out of a few undifferentiated cells left in the wreckage. The time required for this wonderful reorganization is amazingly short. Many maggots transform into adult flies in less than a week, and some mosquito larvæ transform into perfect mosquitoes in less than 24 hours.

The phylogenetic significance of the larval and pupal stages is interesting. Does a metamorphosing insect, in its larval and pupal phases, recapitulate stages in its ancestral development, as do so many other animals? In some respects the larvæ do, but the pupæ probably do not — the exigencies of life have modified the normal course of development. If a flea hatches in a worm-like condition, which may reasonably be considered as a reflection of an ancestral condition of the race, it must adapt itself to the immediate conditions in which it finds itself in order to survive in the struggle for existence; it must and does develop along lines which make it a successful worm before it can proceed with the business of becoming a successful flea, and the requirements are very different. The demands of nature are carried so far that the final development into a flea is accomplished more easily by starting all over again than by attempting to remodel a trash-gnawing, grovelling worm into a blood-sucking, jumping flea. The intervening pupal stage of transformation, therefore, corresponds to nothing in the phylogenetic history of the flea; it is a new and highly specialized modification in the life cycle, developed as a means of overcoming a situation which would otherwise present great difficulties.

The length of life of insects in the larval and adult stages varies with almost every species and with environmental conditions. The larval stage may occupy a small portion of the life, as in the case of many mosquitoes and flies, or it may constitute the greater part of it. There are some mayflies, for instance, which live the greater part of two years as larvæ but exist as adults not more than a few hours. As a rule male insects are shorter lived than the females; the length of life of the latter is determined by the laying of the eggs — when all the eggs have been laid the female insect has performed her duty in life and is eliminated by nature as a useless being. The result is the paradoxical fact that ideal environmental conditions *shorten* the life of these insects, since they facilitate the early deposition of the eggs.

Classification. — The classification of insects is based mainly on three characteristics: the type of development, the modification of the mouthparts, and the number, texture and venation of the wings. All blood-sucking insects have mouthparts adapted in some way for piercing and sucking, but the types vary greatly in different groups. Many of the more thoroughly parasitic insects, *e.g.*, lice, bedbugs and "sheep ticks," have secondarily lost their wings entirely, or have them in a rudimentary condition. In the whole order of Diptera the second pair of wings is reduced to inconspicuous club-shaped appendages known as halteres.

Of the twenty-five orders of insects which are listed by Comstock, only five are of interest as parasites, namely the Hemiptera, or true bugs; the Mallophaga, or bird lice; the Anoplura, or sucking lice; the Siphonaptera, or fleas; and the Diptera, or two-winged flies. Of these the Mallophaga may be omitted so far as human parasites are concerned. The four remaining orders may be briefly summarized as follows:

Hemiptera: metamorphosis incomplete; mouthparts fitted for piercing and sucking, the piercing organs being ensheathed in the jointed lower lip; first pair of wings, unless reduced, leathery at base and membranous at tip; second pair of wings, when present, membranous with relatively few veins. Human parasites: bedbugs, cone-noses, kissing bugs.

Anoplura: metamorphosis incomplete; mouthparts fitted for piercing and sucking, and retractile into a pouch under pharynx; wings secondarily lost. Human parasites: sucking lice.

Siphonaptera: metamorphosis complete; mouthparts fitted for piercing and sucking, the piercing organs being ensheathed in the labial palpi, and the maxillæ modified as holding organs; wings secondarily lost. Human parasites: fleas, chiggers.

Diptera: metamorphosis complete; mouthparts fitted for piercing and sucking, for sucking alone, or rudimentary; first pair of wings (absent in a few species) membranous with few veins; second pair of wings represented only by a pair of clubshaped organs, the halteres. Human parasites: sandflies, mosquitoes, midges, blackflies, gadflies, tsetse flies, stable-flies, maggots.

CHAPTER XXI

THE MITES

General Account. — The mites and ticks, which constitute the Order Acarina of the Class Arachnida, are only slightly known by the majority of people. Popular knowledge of them is usually limited to a few species of ticks, chicken mites, and perhaps two or three other species of mites. Yet the group includes a large number of species, varying in size from some ticks which are half an inch or more in length to mites barely visible to the naked eye. The variety of body form is great and some species when magnified appear ridiculously grotesque. The majority of the species are more or less round or oval, with head, thorax and abdomen all in one piece, but many have the cephalothorax (head and thorax fused together) distinctly marked off from the abdomen, while a few are quite wormlike in form. Many mites are free-living and prey upon decaying matter, vegetation, stored foods and the like; some are predaceous and feed upon smaller animals; some are aquatic, even marine; and many are parasitic on other animals during all or part of their life cycle, and some of these serve as intermediate hosts for, and for dissemination of, dangerous disease germs.

Like other Arachnida (spiders, scorpions, etc.) the mites and ticks usually have two pairs of mouthparts and four pairs of legs, though the last pair of legs is not acquired until after the first moult. The first pair of mouthparts, or cheliceræ, are sometimes needle-like, sometimes shaped like a grapnel hook, and very often pincer-like, the pincers often being at the tip of a long exsertile needle-like structure. The second pair of mouthparts, or pedipalps, are simple segmented palpi. In many kinds of Acarina the anterior end of the ventral side of the body is produced as a sort of chin or lower lip, the hypostome, which may be needle-like or barbed and rasplike (Fig. 194).

The digestive tract is in most cases well developed. Waves of muscular contraction make a very efficient sucking organ of the pharynx. The stomach has pouches opening from it which act as food reservoirs (Fig. 191), so that one meal may last for a long time. The intestine is usually short and the excretory organs, malpighian tubules, open into it not far from the anus. The reproductive organs, as in other Arachnida, open on the ventral surface of the abdomen but at different places in different species. The nervous system is largely concentrated into a great mass, the "brain," lying near the anterior end of the body and pierced by the esophagus. Many mites possess tracheæ, similar to those of spiders and insects, for breathing, while others, soft-skinned forms, simply absorb oxygen through the surface of the body.

Life History. — The life histories of mites and ticks are somewhat variable, but usually there are four stages in their development: the egg, the larva, the nymph and the adult (see Fig. 203). The eggs are usually laid under the surface of the soil or in crevices, or, in some parasites, under the skin of the host. After a varying period of incubation, which depends on climatic conditions, the larva hatches in the form of a six-legged creature, often quite unlike the parent. After a single good feed of blood or plant juices the larva rests, sheds its skin and appears with an additional pair of legs and a body form more closely resembling that of the parent but without developed sexual organs. The nymph thus produced feeds again, sheds its skin from one to three times and finally, after another period of rest during which its body is remodeled for the second time, moults again and comes forth as a fully adult male or female, ready for the reproduction of another generation. There are all sorts of modifications of this order of development, due to the slurring over of one phase or another. One of the most aberrant species is the louse-mite, *Pediculoides*. In this form the eggs develop within the parent's body and the adult males and females issue forth from the brood chamber improvised for them out of the abdomen of the mother (Fig. 179).

The popular opinion that all mites are parasitic is, as remarked before, far from being true. Over half of the known species are not parasitic at any stage in their life history, while many others are parasites only during part of their life cycle.

Parasitism. — The mites are an interesting group for the study of the origin of parasitic habits since, as Ewing has shown, parasitism has apparently arisen independently in different families and genera at least eleven times. Nathan Banks in his treatise on the Acarina, after giving a number of interesting examples of peculiar parasitic habits, writes as follows: "We can only explain these remarkable habitats by the fact that mites, especially in their immature stages, have an incontrollable desire to go somewhere, and get into every cavity and crack they discover in their wanderings. When hungry they test their locality for food, and if not too different from their previous diet this new habitat may result in new species and genera."

A few species of mites have become adapted to live as internal parasites and there are records of mites which are not normally parasitic at all living and multiplying in the human urinary bladder, but all the species normally infesting man are either external or subcutaneous in their operations. A few of the species which are not averse to human beings as food are troublesome and irritating enough to bring their whole tribe into disrepute. The families of Acarina which contain species annoying to man are the *Ixodidæ* and *Argasidæ,* the ticks; *Trombidiidæ,* the harvest mites and " red bugs "; *Parasitidæ* (*Gamasidæ*), including the chicken mites; *Pediculoididæ,* including the louse-mite; *Tyroglyphidæ,* including the cheese and grain mites; *Sarcoptidæ,* the itch mites; and *Demodecidæ,* the hair follicle mites. For convenience we may include with the mites the very aberrant Pentastomida or tongue-worms. Since the ticks are popularly looked upon as quite distinct from other Acarina, and form a very important group of the order on account of their rôle as disease carriers, they will be considered in a separate chapter.

Harvest Mites

The six-legged larvæ of the harvest mites, family Trombidiidæ, known as red-bugs or chiggers, are very annoying pests, and some species have been proved to be the carriers of a typhus-like disease in the Far East. Harvest mites are little scarlet-red animals, and their larvæ are tiny creatures barely visible to the naked eye, usually some shade of orange or red in color (Fig. 176). According to one writer who had evidently experienced them a red-bug is a " small thing, but mighty; a torturer — a murderer of sleep; the tormentor of entomologists, botanists and others who encroach on its domains; not that it bites or stings — it does neither; worse than either, it just tickles."

The adult harvest mites (Fig. 177) are law abiding members of the community, and attack only such animals as plant-lice, caterpillars and other insects. They hibernate in soil or sheltered crevices and in the spring lay their eggs, several hundred apiece, in the ground or among dead leaves. The eggs are very small, round and brownish in color, and were once classified as fungous growths! The newly hatched six-legged larvæ remain close to the ground or creep up on blades of grass or plant stems or in some species into bushes and await an opportunity to attach themselves to a host. If successful in finding a host, or rather in being found by a host, the mites gorge themselves, then drop to the ground, crawl to some snug hiding place and undergo a transformation. The whole inside of the body is remodeled, a fourth pair of legs is acquired, and after a few weeks the skin is shed and an adult trombidiid mite crawls forth.

The appearance of the larval mites may be seen from Fig. 176. They are so minute in size as to be visible only on very close inspection; the average length, when unfed, is about 0.25 mm. with a width of about 0.15 mm. The body is ovoid in form, with three pairs of relatively long six-jointed legs. On the back, just behind the head, is a dorsal shield or scutum more or less rectangular in shape, with five feathered hairs and two long sensory hairs. Both dorsal and ventral sides of the abdomen, the palpi, and the legs are also provided with feathered hairs. The shape of the dorsal shield and the form, length and arrangement of the hairs are used in distinguishing the species.

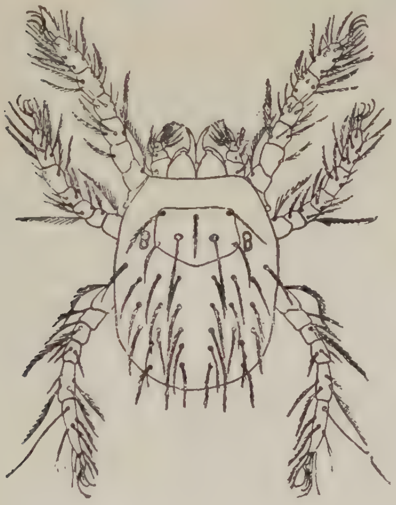

Fig. 176. European red-bug, the larva of *Trombicula autumnalis*. × 150. (After Hirst.)

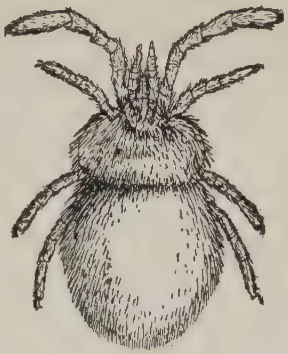

Fig. 177. An adult of the kedani mite, a Trombidiid. × 40. (After Nagayo *et al.*)

When a human being comes in contact with larvæ which are hungrily waiting for their first meal, the larvæ, if of a species for which a human meal is acceptable, attach themselves to his body or clothing. They are so small that they can easily creep through the meshes of ordinary clothing and reach the skin, where they firmly attach themselves, setting up the characteristic severe irritation and intense itching. Usually the skin swells up into a hard, raised area in the vicinity of the bite, which in some individuals is much more pronounced than in others. The mites do not burrow into the skin, but often attach themselves at the mouth of hair follicles. They remain attached for several days, engorge like ticks, and then drop off.

It was formerly thought that larval harvest mites normally fed on insects as do the adults, and only abnormally and accidentally attacked vertebrates, but this has been found to be untrue. The larvæ not only normally attack vertebrates but often have decided preferences. Thus the American species, *Trombicula irritans*, according to Ewing, does not often attack small rodents such as rats or mice, but is extremely fond of rabbits and unfortunately of man and many domestic animals, and it also infests reptiles and ground birds; one California species chooses tree-frogs; most of the Japanese species show a preference for field mice; and one New Guinea species, *Schöngastia vandersandei*, is found abundantly on the heads of Goura pigeons. Species of the related genus *Hannemania* encyst under the skin of amphibians.

The irritation caused by the mites is probably due to a specific poison secreted by the mites rather than to any wounds that they make. The inflammation of the skin may not be felt for 12 or even 24 hours after infection by the mites. When the inflammation does commence there appear large red blotches on the affected parts of the body which itch intensely and are made worse by scratching. After a day or so the red blotches blister and finally scab over. It appears likely that in addition to irritating the skin, red-bugs also produce a toxic substance which affects the nervous system, causing such symptoms as insomnia, lethargy, irritability, etc., and not infrequently a very considerable fever.

Red-bug rash is most frequent on tender-skinned people and on those parts of the body which are most exposed, though it may spread over the whole body and torment the victim unbearably. One individual has informed the writer that during some survey work in a locality heavily infested with red-bugs he observed that many of the laborers who rarely took a bath were practically unaffected by the mites while he was very severely attacked. As an experiment he eschewed his bath for two or three weeks, and was then no longer troubled! The apparent immunity of laborers who are continually exposed to these mites, and yet suffer little if at all from them, may possibly be explained in this manner. In Mexico a species known by the Aztec name "tlalsahuatl" meaning " grain of earth," now thought to be identical with the common North American red-bug, is said to show a decided preference for the eyelids, armpits, groins and other thin-skinned portions of the body, where it induces itching and inflammation, and even ulceration when scratched. The " bête rouge " or " colorado " of the West Indies and Central America is a similar if not identical species.

Sprinkling sulphur on the legs and inside the stockings is a necessary preventive measure for those who are seriously affected by red-bugs, and who have to walk through tall grass or brush where these pests abound. A hot bath shortly after infection, with soap or with soda in it, gives much relief. Some susceptible individuals find that a bath with baking soda or ammonia in the water, even if taken some hours after exposure, is a complete protection, but this is not effective in all cases. To allay the itching weak ammonia or baking soda applied to the affected parts is good, and alcohol, camphor and other cooling applications are also useful. In the writer's experience mentholatum is very effective when rubbed on the bites.

For a long time none of the adults of the parasitic larval harvest mites were known, and these pests were generally placed in a separate genus *Leptus*. The common European species was known as *Leptus autumnalis* and the American one *Leptus irritans.*

The larval mites are placed by Oudemans in four genera, *Trombicula, Schöngastia*, *Leeuwenhoekia* and *Hannemania,* which differ only in minor details concerning principally the bristles.

Although in some instances the adults are still unknown, in those instances in which they have been reared the parents of the larval harvest mites have been found to be species of the genus *Trombicula*, which have a velvety coat of dense feathered bristles, which may be either red or colorless. The adult Trombiculæ are readily distinguishable from all other related mites by having a waist-like construction of the body slightly in front of the middle.

Red-bugs have a wide distribution, and species annoying man are found in Australia, Japan and the East Indian Islands, in Europe, and in North and South America. Strangely enough they do not appear to occur in any part of India or Burma; the writer, who is unfortunately very susceptible to their attacks, never experienced them in extensive travels in all parts of these countries. As yet there appear to be no records of them in Africa.

In the United States only one species commonly attacking man, *Trombicula irritans*, is known. It is widely distributed in southeastern states north to Virginia and Maryland, and occasionally as far as New Jersey and Pennsylvania, and it also occurs throughout a large part of the Mississippi Valley. It is particularly common in the Gulf states, especially near the coast, and is believed by Ewing to be identical with the " tlalsahuatl " of Mexico. Other species of *Trombicula* have been described locally in North America but are not known to attack man or domestic animals. The common red-bug appears to attack a considerable variety of mammals, and also ground-birds and such reptiles as turtles and snakes, but rabbits appear to be favorite hosts, and according to observations of the writer in southeastern Texas, the local abundance of this pest is largely correlated with the abundance of rabbits.

In South and Central America several species of adult Trombiculæ have been described, but their relation to the red-bugs infesting man has not been determined. These insects have been recorded as adding materially to the discomforts of life in Central America, Guiana, the Peruvian highlands and Brazil, and this is probably true over a large part of tropical South America.

In Europe red-bugs or harvest mites, particularly *Trombicula autumnalis* (Fig. 176) are well known pests, especially in Central and Western France, where they are known as " bêtes rouges " or " rougets." They are said to attack small mammals, such as rodents, by preference. Whereas *T. autumnalis* is particularly annoying in the fall months, other species, the identity of which is still in doubt, attack principally in the summer months.

A species attacking man, particularly the eyelids and armpits, and causing great irritation has been described from New South Wales, and named *Leeuwenhoekia australiensis.* It is active throughout the Australian summer.

Another species, the scrub itch mite, *T. hirsti*, interferes with human comfort in Queensland; it is very abundant in the nesting mounds of the " scrub-fowl," which, as Sambon remarks, adopted the artificial incubation of eggs long before the ancient Chinese and Egyptians.

It is in Japan and other parts of the Far East that harvest mites are particularly important, since here they are transmitters of a typhus-like disease known as tsutsugamushi disease or flood fever (see p. 191). Japanese investigators have found six different species of *Trombicula* larvæ on field mice in Japan, but only one, *T. akamushi* appears to attack man and it alone, therefore, is concerned in disease transmission. These larval mites occur in countless numbers on the local field mice or voles, *Microtus montebelloi*, living especially on the inside of the ear. The disease-transmitting species occurs only from June to October. They frequently attack the farm laborers who engage themselves in harvesting and handling the hemp which is raised on the flood plains of certain Japanese rivers. It is among these people that the tsutsugamushi disease or flood fever occurs, always following the bite of a mite. The bite, usually in the armpits or on the genitals, is at first painless and unnoticed (unlike American and European red-bugs!), but the mite remains attached at the wound from one to three days before dropping to the ground to transform to the nymphal stage. The bite of the mite is said to develop into a tiny sore or inflamed spot, in the region of which the lymph glands become swollen and painful, and flood fever follows. According to Nagayo *et al.*, since the larval mite does not usually suck on two animals successively during its life, it undoubtedly acquires the virus by ovarian infection from its parents. The nymphs and adults are infective as well as the larvæ, but are not involved in disease transmission because they do not attack warm-blooded animals. In central Japan the mites usually pass the winter in the adult state, deposit their eggs in soil in late May, and to some extent throughout the summer, and appear as larvæ only during the summer months; in Formosa they are present from March to November.

In some of the East Indian islands red-bugs seem to constitute a more intolerable plague than anywhere else, and are described with much feeling by various travelers in these islands. Two species, *Trombicula wichmanni* and *Schöngastia vandersandei*, are very common. Unlike the American species, which occurs almost always in grass, the latter of these two occurs on bushes and low trees, from which it is brushed off by passers-by; it occurs in large numbers on the heads of Goura pigeons, attached in regular rows " like cobble stones on street pavements." The adults of these mites are not certainly known. Around Deli, Sumatra, nine species of Trombiculæ have been found, infesting mammals and birds, and several of them attack man. One of them, *T. deliensis*, has been proved to be the carrier of a disease called pseudo-typhus, which is either identical with or closely related to Japanese flood fever.

There are records, both ancient and modern, of a typhus-like disease in South China, transmitted by " sand mites," which are red-bugs, and there are a few records of typhus-like disease in Indo-China and Malaya. It has been suggested that " Mossman Fever " of North Australia may also be a mite-transmitted disease of similar nature; the mite thought to be involved is *Trombicula hirsti*.

Other Occasionally Parasitic Species

There are many species of mites, of several different families, which under abnormal circumstances or by sheer accident may become troublesome parasites of man. Nearly all mites secrete salivary juices which have a toxic effect when injected into the tissues; therefore any mite which will bite man under any circumstances may become a pest. In nearly all cases the symptoms of attacks by mites are similar — hivelike or rashlike eruptions of the skin, intense itching and in severe attacks fever.

Louse-Mite. — Among the most important of the occasionally parasitic mites are the louse-mites, *Pediculoides ventricosus* and *P. graminum* (Fig. 178), belonging to the family Pediculoididæ. These are very minute species, barely visible to the naked eye, which are normally parasitic on grain-moth caterpillars and other noxious insects, and therefore beneficial. These mites live in stubble, stored grain and beans, cotton seeds, straw, etc., attacking the various insects which infest these products and becoming numerous in proportion to the abundance of their prey. The female has the remarkable habit of retaining the eggs and young in her abdomen until they have become fully developed males and females. Her abdomen in consequence becomes enormously distended so that the rest of the body appears as only a tiny appendage at one side of it. A gravid female (Fig. 179) fully distended may reach a diameter of 1.5 mm., whereas normally she measured only 0.2 mm. in length. Under the most favorable conditions only six days may elapse from the time the young females emerge from the mother before they reproduce a brood of their own. The brood varies in number from a few dozen to over 200.

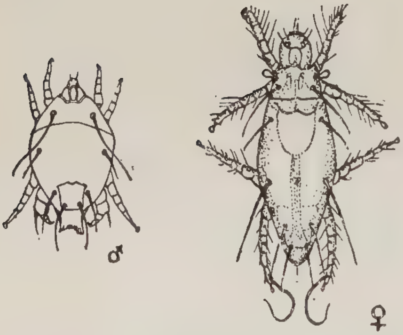

Fig. 178. Louse-mite, *Pediculoides ventricosus;* ♀, unimpregnated female; ♂, male, × 150. (♀, after Brucker from Webster; ♂, after Banks.)

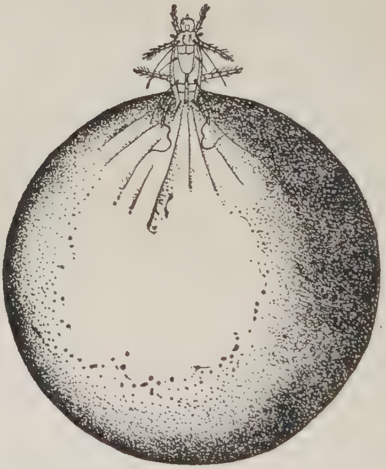

Fig. 179. Louse-mite, gravid female. × about 75. (After Brucker from Webster.)

Like many other beneficial things, these predaceous little mites may become a distinct nuisance, and many serious outbreaks of infestation of human beings by them are on record, especially among the grain threshers of the central portion of the United States and among laborers who handle stored grains and other dry foods. In our Middle West their attacks have often been attributed to harvest mites. In Italy the rash produced by louse-mites is called "miller's itch." Several outbreaks have occurred in the United States due to the use of new straw mattresses. The transformation of all the grain-moth caterpillars into moths leaves the mites with their normal food supply cut off, and they are then ready to feed upon any flesh to which they may have access in an effort to prevent starving to death. It has been suggested that a typhus-like disease observed near Adelaide, Australia, apparently associated with wormy grain, may be transmitted by *Pediculoides*.

The itching rash produced begins about 12 to 16 hours, sometimes earlier, after exposure to the mites. At first they produce pale hivelike spots, which later become red and inflamed, and itch unbearably. Little blisters, the size of a pinhead or larger, appear at the sites of the bites and these later develop into little pustules. Scratching results in the formation of scabs, and when these fall off dark spots which are slow to fade are left on the skin. The rash and itching normally disappear within a week unless fresh detachments of mites are constantly acquired. In severe infestations the irritation and poisoning is sufficient to cause constitutional symptoms such as fever, high pulse, headache, nausea, etc.

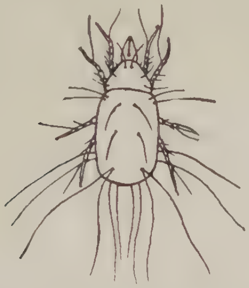

FIG. 180. Grain mite, *Tyroglyphus longior*. × 30. (After Fumouze and Robin.)

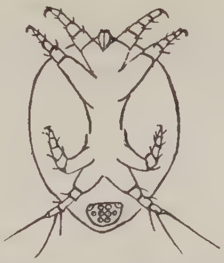

FIG. 181. Hypopus or traveling stage of *Tyroglyphus*, ventral view. Much enlarged. (After Banks.)

Since the mites cannot thrive on human blood, and remain attached to the skin for only a short time, no treatment for destroying them is necessary. Remedies to relieve the itching, such as the application of soda or soothing ointments, or warm baths with a little soda, are called for. Preventive measures which have been suggested include greasing of exposed parts of the body, followed by a change of clothes and a bath after working with infected material, and the powdering of the body with dry sulphur. Control of the mite consists largely in keeping grain and other dry produce as free as possible from the insects on which the mites feed. Burning stubble in winter and threshing wheat directly from the shock would tend to lessen the worms in stored wheat and with them the mites.

Grain Mites. — The family Tyroglyphidæ, including many species of mites which normally feed on grain, flour, sugar, dried fruits, cheese and other foods, contains several species which become annoying to man and produce an itching rash on people who handle infested goods.

According to Banks all the members of this family are pale-colored, soft-bodied mites, with prominent pincer-like cheliceræ and no eyes. Their bodies are about twice as long as wide and are furnished with a few scattered long hairs (Fig. 180).

The life history of some members of the family is quite remarkable in that there is added a phase of existence which does not occur in other mites. All the species scatter their eggs haphazard over the infected material. Upon hatching the larvæ have six legs and acquire a fourth pair after moulting, in orthodox mite style. Some now develop directly into adults, while others go through what is called a " hypopus " stage. The hypopus (Fig. 181) is very different from the nymph from which it develops: the body is hard and chitinous, there is no mouth or mouthparts, the legs are short and stumpy, and there is usually a raised area on the ventral surface with a number of tiny sucking discs. By means of these suckers the hypopus attaches itself to insects or other creatures and is thus transported to new localities, the entire object of the hypopus stage apparently being to secure passage to new breeding grounds. They have frequently been mistaken for parasites, but they are no more parasitic than a man is when on horseback. After dropping from its unwilling transporter the hypopus moults into an eight-legged nymph again, which, after feeding, develops into an adult.

The Tyroglyphidæ are all quite similar in appearance, and the characters which separate the species, and even the genera, are few and minute. A considerable number of species may attack persons who handle infested materials, and they are the cause of " grocers' itch." This affliction is caused especially by various species of *Glyciphagus* and *Tyroglyphus.* Of historical interest is a case of dysentery apparently due to a *Tyroglyphus*, *T. longior*, (Fig. 180) which occurred in one of Linnaeus' students. The mites were abundant in his feces, and were found to live and multiply in a juniper-wood cup which he used. As shown by Castellani, an itching rash known as " copra itch," occurring among the laborers in the copra mills of Ceylon where cocoanut is ground up for export, is caused by a variety of this mite, called *T. longior castellanii.* Copra itch occurs also among stevedores who handle copra in London. Another species, *Glyciphagus buski*, was taken from beneath the skin on the sole of the foot of a negro in England; it had caused large sores. The negro attributed the affliction to the wearing of a pair of shoes loaned him by a similarly affected negro from Sierra Leone, Africa. Another species, *Rhizoglyphus parasiticus*, which lives on roots, bulbs, etc., in India, produces a skin disease among coolies working on tea plantations. It begins with blisters between the toes and spreads to the ankles, causing very sore feet.

Cases of parasitism of the intestine and urinary tract with mites of the families Tyroglyphidæ and Tarsonemidæ are not infrequent. Eggs of mites are not infrequently found in human feces when floatation methods are used for detection of worm eggs, and often mites also are found. As a rule both the mites and the eggs may be considered as having been ingested with food, and passed through the digestive tract without establishing themselves, but that they do occasionally establish themselves at least temporarily, and multiply in the alimentary canal, cannot be doubted. A considerable number of cases of infection of the urinary tract have been recorded. Some of these records are undoubtedly due to contamination of the urine from mites in the bottles or elsewhere, but there no longer seems to be any doubt of the occurrence of true parasitism of the bladder and ureters by mites of the families Tyroglyphidæ and Tarsonemidæ. The result of the infection is an irritation of the urinary tract, one of the commonest symptoms being uncontrollable nocturnal enuresis. The urine usually contains large sheets of epithelial cells, and may have a dark-colored deposit. Mites in various stages of development, and their eggs, are intermittently found. Mites also sometimes establish themselves in the canal of the external ear, and occasionally even penetrate to the inner ear and mastoid.

Other Species. — A few species of the family Tetranychidæ, including the " red spiders " or spinning mites, occasionally become troublesome to man, although they are normally vegetable feeders and may do much damage to cultivated plants. One species especially, *Tetranychus molestissimus,* which lives on the undersides of leaves of a species of cockle bur, *Xanthium macrocarpum,* in Argentina and Uruguay, attacks man during the summer months from December to February. It produces symptoms similar to those of the louse-mite, with intense itching and some fever. The common " red spider," *T. telarius,* an almost cosmopolitan species, also is reported to attack man occasionally.

The common chicken mite, *Dermanyssus gallinæ,* belonging to the family Parasitidæ (Gamasidæ), frequently causes much irritation and annoyance to those who come in contact with it. Although it can thrive and multiply only on certain kinds of birds, it sometimes remains on mammals for some time, causing an eczema or rashlike breaking-out on the skin, attended, as in other mite infection, by intense itching. Except in cases of constant reinfection chicken mites are usually troublesome to man for only a few days at most. Since these mites can live for several weeks without feeding on their normal hosts, places formerly frequented by fowls may be infective after the removal of the birds. Recently the London Hospital was literally dusted with these mites originating from pigeon nests in the roof. The mites normally remain on their hosts only long enough to fill up on blood, usually at night, spending the rest of the time in cracks and crevices in and about the coops. Various sprays of sulphur, carbolic solutions and oils are used to destroy them. An allied species, *Holothyrus coccinella,* living on geese and other birds on Mauritius Island, attacks man, causing burning and swelling of the skin, and frequently proves quite dangerous to children by entering the mouth.

A very small mite, *Tydeus molestus,* belonging to the family Eupodidæ, attacks man in much the same manner as do the harvest mites. It is common on some estates in Belgium, apparently having been imported many years ago with some Peruvian guano. It appears regularly each summer on grass plots, bushes, etc., in great numbers, disappearing again with the first frost. It causes great annoyance in red-bug fashion, not only to man but to other mammals and birds as well.

Itch Mites

The itch mites, belonging to the family Sarcoptidæ, are the cause of scabies or mange in various kinds of domestic and wild animals, and of "itch" in man. This disease is one which has been known for a very long time but was formerly supposed to be caused by "bad blood" or other constitutional disorders such as cause the growth of pimples. Even at the present time the true cause of the disease is not understood by the majority of people.

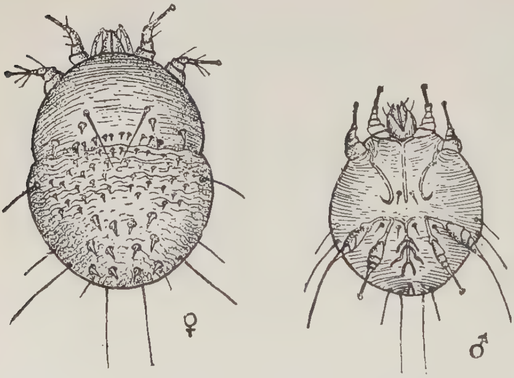

Fig. 182. Human itch mite, *Sarcoptes scabiei;* ♀, female; ♂, male. × about 100. (Partly after Banks.)

The Parasites. — The itch mites (Fig. 182) are minute whitish creatures, scarcely visible to the naked eye, of which the females burrow beneath the skin and lay eggs in the galleries which they make. They are nearly round and the cuticle is delicately sculptured with numerous wavy parallel lines, pierced here and there by stiff projecting bristles or hairs. There are no eyes or tracheæ. The mouthparts, consisting of a pair of minute cheliceræ and a pair of three-jointed triangular pedipalps, are attached to a capitulum or head, as in ticks, this fitting into a groove in the front of the body. The legs are short and stumpy and are provided with sucker-like organs, called ambulacra, at their tips. In the female the two posterior pairs of legs terminate in a simple long bristle, whereas in the male only the third pair of legs terminates in bristles. The human itch mite, *Sarcoptes scabiei*, is only slightly distinguishable from the itch mites which cause scabies and mange in many of our domesticated animals. Many infected species of mammals appear to have their own varieties of itch mites, but many of them can be transferred readily from one host to another. In the human species the male is only about 0.25 mm. in length, while the female is about 0.4 mm. in length. Another species, *Notoedres cati*, which causes a very persistent and often fatal disease in cats, temporarily infests man, but is apparently unable to breed in human skin, since the infection dies out in a week or two.

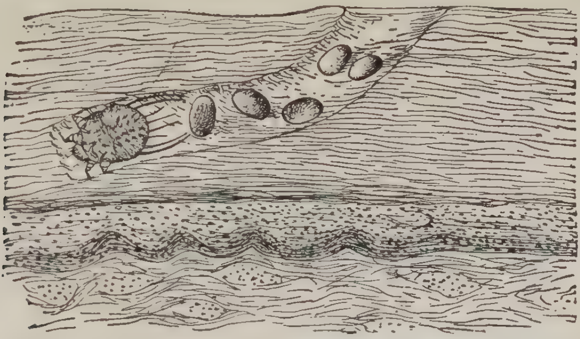

Fig. 183. Diagrammatic tunnel of itch mite in human skin, showing female depositing eggs. × about 30. (Adapted from Riley and Johannsen.)

The impregnated females of itch mites excavate tortuous tunnels in the epidermis (Fig. 183) especially on such portions as between the fingers and toes, on the groins and external genitals, and in the armpits, where the skin is delicate and thin. The tunnels are anywhere from a few millimeters to over an inch in length, and are usually gray in color from the eggs and excrement deposited by the female as she burrows. The daily excavations of a mite amount to two or three millimeters.

The eggs (Fig. 183) which are about 160 μ long, vary in number from 15 to 50. They are laid in groups of from two to four, the mite resting after each oviposition. After they are all laid the female dies, usually at the end of a single tortuous burrow. The eggs hatch in from three to six days into larvæ which resemble the adults except in minor details and in the absence of the fourth pair of legs. The larvæ transform in two or three days into nymphs. The nymphs commonly build burrows for themselves and moult twice, the second time becoming adult male and female mites. The duration of the two nymphal periods is from three and one-half to six days, the entire development of the mites therefore requiring from nine to sixteen days. The mites are not necessarily nocturnal as was formerly supposed, but wander about on the surface of the skin when the latter is warm, which is most frequently the case when the host is in bed. Copulation takes place on the surface of the skin, and apparently the males do not burrow or enter the burrows made by the females, but merely hide under superficial dead cells of the epidermis. Since they die very soon after copulation, they are seldom found. The young impregnated females soon begin fresh excavations, and produce more eggs. Fifteen or twenty eggs each generation, of which approximately two-thirds are females, and a new generation about every four weeks, results in an enormous rate of increase. In less than six months the progeny of one pair of itch mites theoretically would number several millions!

The Disease. — The " itch " is a disease which in the past has swept over armies and populations in great epidemics, but it has decreased with civilization and cleanliness, and is fortunately less common now, at least in civilized communities.

As its name implies, the disease is characterized by itching of the most intense kind where the mites burrow in the skin. The itching is probably due only to a very slight extent to the mechanical irritation in the skin, but is induced rather by poisonous substances secreted or excreted by the mites. Injection of fluid containing crushed mites produces an eruption and irritation similar to that caused by the burrowing of the living mites.

The excretions of the mites as they feed in their burrows form little hard pimples, about the size of a pinhead or a little larger, containing yellow fluid. When these are scratched, as they are almost certain to be on account of the unbearable itching, they frequently become secondarily infected and may give rise to larger sores. Ultimately scabs form over them.

Since the entire life history of the parasites is passed on a single host, generation after generation may develop from a single infection, and although the infection apparently may disappear temporarily, it persists recurrently for many years. Since the mites are sensitive to cold the infected areas of skin not only do not spread but may become restricted during the winter, to spread with renewed vigor with the coming of warm weather. So persistent is the infection that it is doubtful whether it ever spontaneously dies out. A particularly severe form of the disease known as " Norwegian itch " or " crusted itch " occasionally occurs; unlike the ordinary form of the disease it attacks the face and scalp as well as other parts of the body, and gigantic crusts form over the infected parts. Until recently the mite causing this virulent form of the disease was thought to be a distinct variety, called *Scaroptes scabiei crustosæ*, but recent investigations indicate that the parasite is the same as in ordinary itch.

Infection can result only from the passage of male and female mites, or of an impregnated female, from an infected to a healthy individual. Normally this takes place by actual contact, rarely in the daytime on account of the secretive habits of the mites, but commonly at night, especially from one bedfellow to another. Gerlach experimented to determine how long the mites could live away from their hosts and found that in the dry warm air of a room they lost vitality so rapidly that they could not be revived after three or four days. In moist places, on the other hand, such as in the folds of soiled underwear or bedcloths, they survived as long as ten days. From this it is evident that infection may take place by means of bedding, towels, underwear or other cloth which may come in contact with infected skin. The author once witnessed an epidemic of itch arising from the use of an infected wrestling mat in a college gymnasium. It is also possible for infection to be derived from mangy animals, though the mites, once adapted for several generations to a given host, do not often survive a transfer to a different species of host more than a few days.

Treatment and Prevention. — The treatment of itch before the nature of the malady was understood was considered very slow and difficult, and even at the present time it is looked upon by many people as a disease which can be recovered from only after prolonged treatment. The fact that the mites burrow beneath the skin to lay their eggs makes careless superficial treatment almost as inefficient as the internal medicine which was once taken to " purify the blood." The most effective treatment for the itch is as follows: the patient rubs himself vigorously with green soap and warm water for about 20 minutes, and follows this with a warm bath for half an hour or more, during which the soapy massage continues. In this manner the skin is softened, the pores opened and the burrows of the mites soaked so that the application of mite poison which is to follow will penetrate more readily. When the skin is thus prepared some substance for destroying the mites is applied. Sulphur ointment made by mixing one-half an ounce of sulphur to ten ounces of lard, is excellent; its virtue lies in the formation of hydrogen sulphide in contact with the skin, sulphur itself being inert. A still more efficient though more expensive remedy is a beta-naphthol ointment, prepared as follows: beta-naphthol, 75 grains; olive oil, $2\frac{1}{2}$ fluid grams; sulphur, 1 oz.; lanolin, 1 oz.; green soap, 1 oz. One of these applications, or some other, is unsparingly rubbed into the skin of the infected portions of the body, and of a considerable area around them. When rubbed in for 20 or 30 minutes the patient goes to bed, leaving the ointment on his body until morning when it is washed off in another bath. Meanwhile the soiled underwear, bedclothes or other possibly infected articles are sterilized by boiling or baking. Since this course of treatment does not destroy the eggs it is repeated in about ten days in order to destroy any mites which may have hatched in the meantime.

For delicate-skinned individuals the treatment described above is too severe and may, of itself, give rise to inflammation of the skin not unlike that caused by the mites. In such cases balsam of Peru may be used satisfactorily instead of sulphur ointment, but should be rubbed in several times at intervals of a few hours. It does not cause any irritation.

Prevention of this annoying infection consists merely in avoiding contact with infected individuals, and of shunning public towels or soiled bed linen. A single infected individual in a logging or railroad camp may be a means of infecting the entire camp. Means should, therefore, be taken to guard against such individuals whenever possible, and to prevent the spread of infection from unsuspected individuals by care as regards the use of towels and bed clothes.

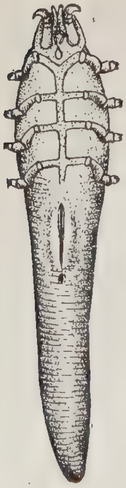

FIG. 184. Hair follicle mite, *Demodex folliculorum*. ×200. (After Mégnin.)

Hair Follicle Mites

The hair follicle or face mite, *Demodex folliculorum* (Fig. 184), of the family Demodecidæ, is a species which is most strikingly adapted for its parasitic life. It is a wormlike creature, very unmite-like in general appearance, which lives in the hair follicles and sebaceous glands of various mammals. In man it occurs especially on the face. Numerous forms from various animals have been described as different species, but they are all strikingly alike and the extent of their specificity is questionable.

The wormlike appearance of the adult mites is due to the great elongation of the abdomen which is marked by numerous fine lines running around it. The head is short and broad, and the four pairs of legs, all similar, are short, stumpy, three-jointed appendages. The female mites are .35 to .40 mm. long, while the males are a little smaller.

The multiplication of these mites is slow. The eggs hatch into tiny six-legged larvæ in which the legs are mere tubercles. It requires four moults to bring the larvæ to sexual maturity.

In most cases these parasites cause no inconvenience whatever in man and their presence is not even suspected, although in many domestic animals they cause severe types of mange. It has been suggested that in some cases the mites may carry bacteria into the skin and be the cause of a form of " ring " impetigo. In Europe a large proportion of people are said to be infected, but in America, according to Riley and Johannsen, there is reason for believing that the infection is far less common than is usually supposed. Since generation after generation may be produced on a single host the infection is potentially indefinite in its duration. When the mites become numerous in the hair follicle or sebaceous glands they sometimes cause "blackheads" by causing a fatty accumulation to be produced, but they are not the only or even the usual cause of " blackheads." The skin disease known as "acne" has also been attributed to these mites, but probably erroneously. Follicle mites have been suspected also of spreading leprosy.

The method of transmission of the mites to another host is not definitely known but it is probable that the adults wander on the surface of the skin at times, and may then be transmitted by direct contact or by towels, as are itch mites. In dogs, where the follicle mite, possibly a different species, causes a very severe and often fatal form of mange, transmission from dog to dog takes place in a very irregular manner, and there are frequent instances cited of infected dogs associating for a long time with uninfected ones without spreading the disease. Experiments with transmission of the canine follicle mite to man have invariably failed. Little is known about treatment of *Demodex* infection, but application of various substances, including sulphur ointment, ether and 1 to 2% iodine, castor oil, etc., have been used with some success in animal infections.

Pentastomida: Tongue worms and their Allies

At one time this aberrant group of arthropods was classified with the Arachnida and was thought to be related to the mites, but they are now usually placed in a separate class. The animals have become so modified by parasitic life that their affinity with the arthropods would be difficult to recognize if it were not for the form of the larvæ, which are more or less mite-like and have either two or three pairs of legs. Even in life cycle they resemble parasitic worms in that they pass the immature stages in an intermediate host. In fact they were at one time or another classified with each of the major groups of parasitic worms.

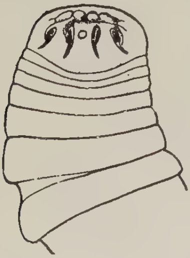

Fig. 185. Head of *Armillifer armillatus.* ×3. (After Sambon.)

The adults have elongate bodies which are either flattened or cylindrical and divided into a series of usually conspicuous rings which are not, however, true segments. There is no distinct division into head, thorax or abdomen. On either side of the mouth at the anterior end there are two pairs of hollow, fang-like hooks which can be retracted into grooves like the claws of a cat (Fig. 185). These are usually looked upon as the vestiges of some of the appendages. At the bases of the retractile hooks there open a number of large glands, the secretion of which is believed to be hemolytic. The internal organization of the body is degenerate in the extreme; there is no blood, no respiratory system, no special sense organs, no organs of locomotion; little more than the barest necessities of existence — a simple nervous system, a usually straight digestive tract and a reproductive system. The anus is at the posterior end of the body. The females, which are larger than the males, have the genital opening either near the anterior or posterior end of the abdomen. The family Linguatulidæ, which include all the forms parasitic in mammals, have a posterior genital opening and a tubular uterus. The genital opening of the males is anterior.

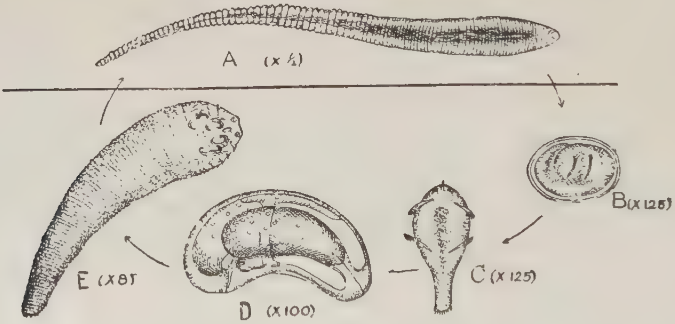

Fig. 186. Life history of tongue-worm, *Linguatula serrata;* *A*, adult female from nasal passage of dog; *B*, egg containing embryo; *C*, larva from sheep, man or other animals; *D*, encysted larva; *E*, 2nd larval stage, from liver of sheep or man. (*A*, after Neumann; *B*, *C* and *D* after Leuckart; *E*, after Railliet.)

The life cycle of one species, *Linguatula serrata*, was worked out by Leuckart many years ago. As a whole the group was much neglected and the classification and identity of species in great confusion until Sambon straightened them out a few years ago.

The eggs (Fig. 186*B*), enclosed in a thin, bladder-like envelope filled with a clear albuminous substance, contain inside the thick shell an embryo with either four or six legs; in the Lingualutidæ there are four. These eggs are voided by the host with the catarrhal products of the respiratory system, the egg-laden mucus infecting water or grass or other vegetation, with which they are eaten by herbivorous animals. The eggs, at least in some species, are very resistant and remain alive for several months outside the body of the host. When ingested by an intermediate host the eggs hatch and liberate the four or six-legged larvæ. In *Linguatula* these are about 75 μ long. The larvæ of this species migrate to the mesenteric ganglia, liver, lungs or other organs and there encyst (Fig. 186*D*). They moult twice and assume a pupa-like stage in which they are devoid of mouthparts, hooks or segments, and have a length of 0.25 to 0.5 mm. A number of other moults follow, and finally, after 5 or 6 months, a nymphal stage is attained, in which the animal possesses two pairs of hooks and a body, 4 to 6 mm. in length, which is divided into about 80 to 90 rings, each bordered posteriorly by a row of closely set spines (Fig. 187). These are shed when the nymph transforms into an adult. For a long time this nymph was looked upon as a distinct species.

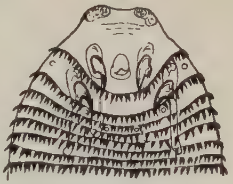

Fig. 187. Head of nymph of *Linguatula serrata*. (After Faust.)

At this stage a " wanderlust " often seizes the animals and they frequently escape from their cysts, falling into the peritoneal cavity, lungs, or even into the lumen of the intestine. The migration in the body appears to be largely passive, but they may possibly sometimes reach the nasal passages and succeed in reaching the adult stage. This might explain the occasional occurrence of the adults in herbivorous animals. Ordinarily, however, the nymphs either remain encysted in the original locations or perhaps re-encyst in other places and reach the final host only when the intermediate host is eaten. Infection of the final host may possibly occur also by the larvæ, which have accidentally escaped with feces or nasal secretions, being snuffed up by the final host.

While a few instances of the adults of *Linguatula serrata* in man are known, human infections are much more frequently due to nymphs which are found encysted in or on the liver, mesenteries, lungs or other organs, or free in the peritoneal cavity.

One of the tongue-worms which is most frequently observed in man, especially in Europe, is *Linguatula serrata*. The male of this species is a small worm, whitish in color, 18 to 20 mm. in length, whereas the female (Fig. 186*A*), which is yellowish or brownish due to the eggs in her body, reaches a length of from 80 to 130 mm. The adults occur in the nasal passages and frontal sinuses principally of dogs (Fig. 188), and occasionally other animals such as herbivores and man, where they suck blood. They cause severe catarrh, bleeding and suppuration. The eggs (Fig. 186*B*) are dispersed with the mucus during the violent fits of sneezing to which the presence of the parasites gives rise. The swallowing of food or drink, especially grass or vegetables, soiled by this infective mucus, or in the case of man too intimate contact with dogs, results in the access of the larva-containing eggs to the intermediate host, which is most frequently sheep, goats, rabbits, etc., but occasionally man. In man the encysted nymphs are most frequently found in or attached to the liver. *L. serrata* is nowhere abundant, even in its normal hosts, though it has a wide geographic distribution; in some parts of Europe, however, adult parasites have been found in 10% of dogs examined, and in some series of autopsies as high as 10% of human beings have been found to harbor the nymphs. Usually, however, they are dead and calcified, and of no pathological importance. Adult parasites in man are rare; there is one instance known in which a frequent bleeding of the nose which had persisted for seven years ceased when an adult *Linguatula* was expelled in a violent fit of sneezing.

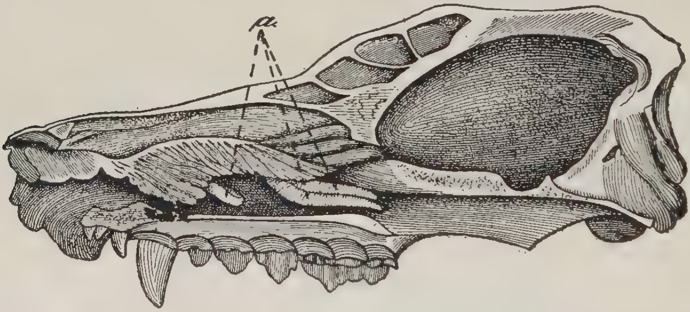

Fig. 188. Head of a dog split in half to show three tongue-worms, *Linguatula serrata*, (*a*) in the nasal cavity. Reduced in size. (After Colin, from Hall.)

Man is also frequently parasitized by the nymphs of at least two species of *Armillifer* (formerly *Porocephalus*). One, *A. armillatus*, is an African species which passes its mature stage in pythons and other snakes, while among the commonest intermediate hosts are various apes and monkeys, although carnivores, antelopes, giraffes and various other animals also become infected. It is significant that monkeys constitute an important article of diet for the African pythons. Since in some parts of Africa the natives esteem python steaks it is not surprising that human infections are common. Infection may, however, occur also by the agency of water or vegetables contaminated by eggs of the worms. Numerous cases have been reported from all parts of West Africa, and Broden and Rodhain have found them in no less than 30 of 133 postmortems in Belgian Congo. In the Oriental Region this species is replaced by a closely related one, *A. moniliformis*, also parasitic in pythons. Several human infections with this worm have been recorded, one from Manila, one from Sumatra, and one from a Tibetan in China.

These two species of *Armillifer* are much alike. They have cylindrical bodies with annulations marked by conspicuous bracelet-like rings giving a screw-like appearance (Fig. 189); they are bright lemon-yellow in color; the females are 90 to 130 mm. long, the males about 30 to 45 mm. *A. moniliformis* is more slender and has more rings than *A. armillatus*. The eggs are elliptical, double-shelled, about 108 μ long by 80 μ wide, and enclosed in a large fluid-filled circular bladder. Experimental infections have been produced by eggs kept under adverse conditions in soil for three months. The nymphs lie coiled up in cysts either imbedded in or attached to the liver or other organs;

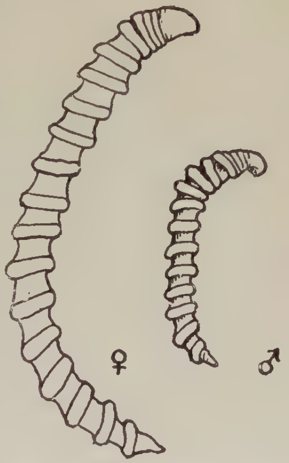

Fig. 189. *Armillifer armillatus;* ♀, female; ♂, male. Natural size. (After Sambon.)

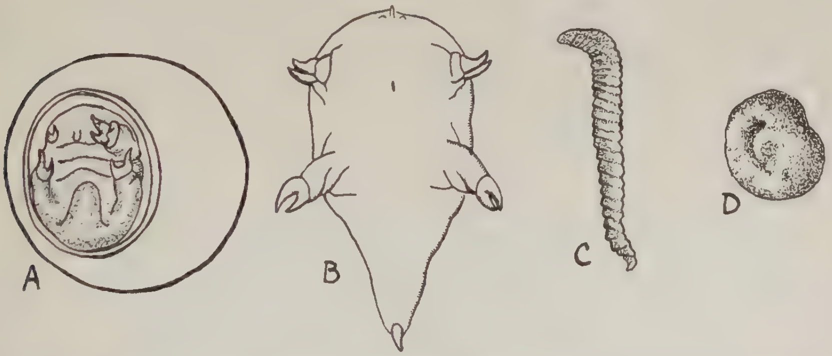

Fig. 190. Stages in development of Porocephalids. *A*, egg of *Porocephalus* with developed embryo, × 280; *B*, embryo of *Armillifer armillatus*, × about 500; *C*, nymph of *Armillifer* pressed out of cyst, × 3½; *D*, encysted nymph of same, × 3½; (*A* and *B* after Sambon; *C* and *D* after Fulleborn.)

they resemble miniatures of the adults. The nymphs, ingested by pythons, burrow through the stomach wall and reach the lungs within three days. In the intermediate host, on the other hand, development is very slow, requiring one and one-half to two years to reach a length of 16 to 22 mm.

Two American cases of infection with Porocephaline worms have been recorded. Since no American species of *Armillifer* is known, it is probable that these cases were due to immature forms of *Porocephalus crotali* of rattlesnakes, or some allied form. *Porocephalus* differs from *Armillifer* in having a smooth annulated body, without conspicuous rings.

It appears that in most cases of infection, when only a few worms are present, very little if any injurious effect is felt from them, but there can be no doubt of their producing serious illness in heavy infections, depending upon the organs which are particularly affected. There are no characteristic symptoms by which the infection can be diagnosed, and it is seldom recognized except at autopsies.

CHAPTER XXII

TICKS

While mites as a group are extremely annoying pests, with the exception of some Oriental species of red-bugs they are not dangerous as disease carriers. The ticks, on the other hand, are not only annoying but dangerous. Several important diseases of domestic animals are transmitted solely by ticks, and several human diseases are likewise dependent on ticks for dissemination, especially African relapsing fever or " tick fever " and Rocky Mountain spotted fever. In addition to this, tick bites, at least those of some species, may give rise to a serious form of paralysis, especially in children, which may end in death. Tick bites also frequently give rise to dangerous ulcerating sores which may result in fatal blood poisoning. The economic importance of ticks as parasites of domestic animals is not for consideration here, but it would not be amiss to state that the annual loss in the United States from cattle ticks alone is estimated at many millions of dollars. It is evident that ticks should be looked upon as worthy candidates for extermination wherever this is possible.

Although the ticks constitute only one of several divisions of the order Acarina, they are so readily distinguishable and so well known that in the popular mind the ticks are looked upon as a group quite distinct from all others of the order, and equivalent with the mites. They are of relatively large size and usually exceed all other Acarina in this respect even in their larval stages. Some species when full grown and engorged are fully half an inch in length.

General Anatomy. — The body of a tick is covered by a leathery cuticle which is capable of great expansion in the females as they engorge themselves on their host's blood, filling the numerous complex pouches of the digestive tract (Fig. 191). When not engorged ticks are flat and oval or triangular in shape (Fig. 196), usually tapering to the anterior end, but after engorgement they resemble beans or nuts of some kind (Fig. 197). Most ticks have a little shield or " scutum " on the dorsal surface, quite small in the females, but nearly or quite covering the back in the males (Fig. 202). Attached to it in front is a little triangular piece, the capitulum or " head " which bears the mouthparts (Fig. 192). The latter consist of a quite formidable piercing organ, the hypostome, a pair of cheliceræ or mandibles which are armed with hooks (Fig. 193), and a pair of blunt palpi which are probably tactile in function. The hypostome is a rasplike structure, beset with row after row of recurved teeth (Fig. 194). So firmly do these hold in the flesh into which the proboscis is inserted that forcible removal of a tick results sometimes in the tearing off of the body from the capitulum which remains attached to the host. Like other Arachnida, ticks have four pairs of legs. These are quite conspicuous when the body is empty but are hardly noticeable after engorgement. The breathing apparatus consists of a system of tracheæ which open by a pair of spiracles in the vicinity of the fourth pair of legs. The shape of the plates which cover the spiracles are sometimes used in distinguishing species. The ventral surface has two openings, the genital pore just back of the proboscis, and the anus some distance from the posterior end of the body (Fig. 196). The presence or absence and arrangement of plates on the ventral side, in the vicinity of the anus, is of considerable taxonomic value.

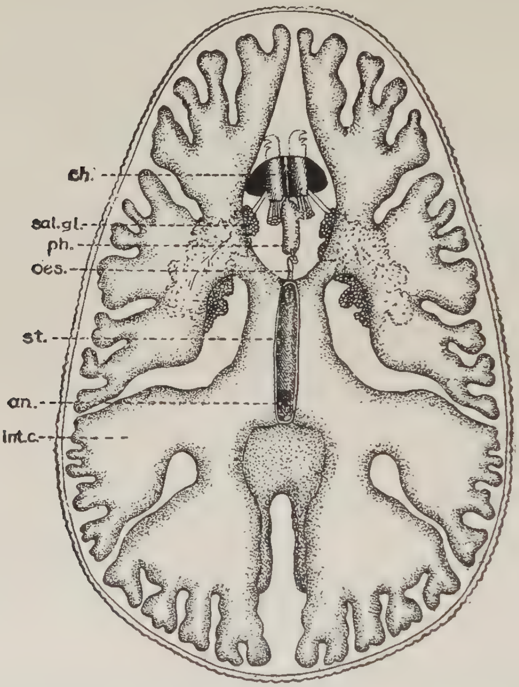

FIG. 191. Digestive tract of *Argas persicus; an.*, anus; *ch.*, chelicera; *int. c.*, intestinal ceca; *oes.*, esophagus; *ph.*, pharynx; *sa. gl.*, salivary glands; *st.*, stomach. × about 20. (Adapted from Robinson and Davidson.)

One feature of the internal anatomy of ticks is of special interest in connection with their relation to disease germs. In the stomach wall there are cells which absorb and assimilate food and then liberate it into the internal body space by actually splitting open. These cells then round up and are shed into the stomach to be expelled as a whitish material with the feces. This unusual mechanism probably facilitates the entrance of germs into the body cavity of the tick, where they can reach the ovaries and eggs and thus be handed on to a subsequent generation, which happens in the case of such widely different germs as spirochætes, rickettsias and some bacteria. Ticks, however, like many other arthropods, possess an anti-bacterial principle in their guts which destroys most bacteria. The bacteria of tularemia, anthrax and, in some cases at least, leprosy can, however, persist for more or less long periods, while others, such as cocci, plague bacilli, typhoid bacilli, etc., fail to become established in ticks.

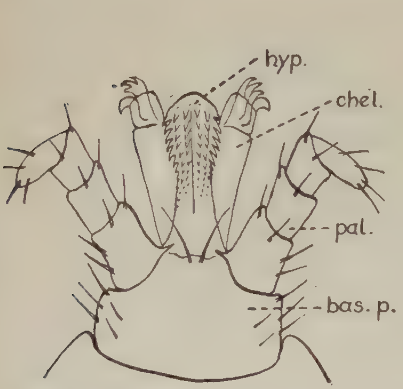

Fig. 192. Head or capitulum of tick; *hyp.*, hypostome; *chel.*, chelicera; *pal.*, palpus; *bas. p.*, basal piece. (Partly after Banks.)

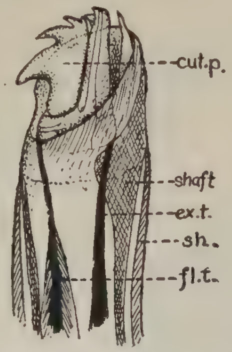

Fig. 193. Tip of chelicera of a tick, much enlarged; *cut. p.*, articulated cutting part; *shaft*, shaft; *sh.*, sheath; *fl. t.* tendon of flexor muscle; *ex. t.*, tendon of extensor muscle. (After Nuttall, Cooper and Robinson.)

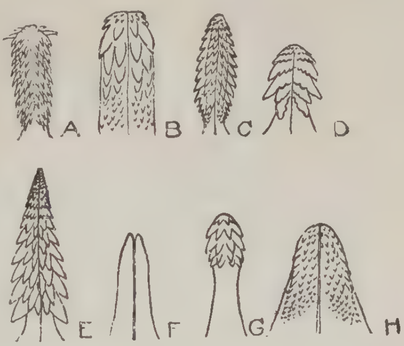

Fig. 194. Hypostomes of ticks; *A*, ear tick, *Otobius* (or *Ornithodoros*) *mégnini*, nymph; *B*, *Argas persicus*, adult; *C*, *Ixodes ricinus*, adult female; *D*, same, male; *E*, *Ixodes vespertilionis*, adult female; *F*, same, male; *G*, *Ornithodoros moubata*, nymph; *H*, *Ornithodoros savignyi*, adult. (*A*, after Salmon and Stiles; others after Nuttall.)

Habits and Life History. — All ticks are parasitic during some part of their lives. The majority of them infest mammals, though many species attack birds and some are found on cold-blooded animals. A very decided host preference is shown by some species, whereas others appear to be equally content with any warm-blooded animal which comes their way. In many species the hosts or parts of hosts selected by the adults are not the same as those selected by the immature forms.

The life histories of all ticks are more or less similar. After several days of mating the female ticks engorge and soon after drop to the ground and begin to lay their eggs (Fig. 195). These are deposited on or just under the surface of the ground. Some of the family Argasidæ engorge several times, laying a batch of from 20 to 50 eggs after each gluttonous repast. All of the Ixodidæ, on the other hand, lay their eggs after a single engorgement. The eggs number from a few hundred in some species to upwards of 10,000 in others and are laid in rather elongate masses in front of the female. Each egg as it is passed out by the ovipositor is coated with a viscid substance by glands between the head and dorsal shield of the tick and is then added to the mass in front. The process of egg-laying occupies several days, as not more than several hundred eggs can be passed out and treated with the viscid coating in the course of a day.

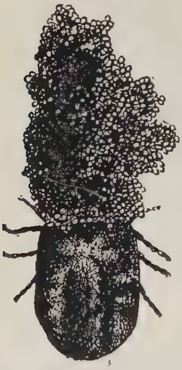

Fig. 195. Texas fever tick, *Boöphilus annulatus*, laying eggs. (After Graybill.)

The eggs develop after an incubation period which varies with the temperature from two or three weeks to several months. Eggs deposited in the fall do not hatch until the following spring.

The larval ticks which hatch from the eggs are much smaller than the adult ticks and have only six legs (Fig. 203*B*). They are popularly known as " seed ticks." The seed ticks soon after hatching climb up on a blade of grass or bit of herbage and assume a policy of watchful waiting until some suitable host passes within reach. Seed ticks must be imbued with almost unlimited patience, since in many if not in the majority of cases long delays must fall to their lot before a suitable host comes their way like a rescue ship to a stranded mariner. The jarring of a footstep or rustle of bushes causes the ticks instantly to stretch out to full length, feeling with their clawed front legs, eager with the excitement of a life or death chance to be saved from starvation. If success rewards their patience, even though it may be after many days or weeks, they feed for only a few days, becoming distended with blood, and then drop to the ground again. Retiring to a concealed place they rest for a week or more while they undergo internal reorganization.

Finally they shed their skins and emerge as eight-legged but sexually immature ticks known as nymphs (Fig. 203*C*). The nymphs climb up on bushes or weeds and again there is a period of patient waiting, resulting either in starvation or a second period of feasting. Once more the ticks drop to the ground to rest, transform and moult, this time becoming fully adult and sexually mature. In this condition a host is awaited for a third and last time, copulation takes place, sometimes even before a final host is reached, and the females begin their final gluttonous feeding which results in distending them out of all proportions. In some species, especially those which live on hosts which return to fixed lairs, copulation takes place off the host. When this occurs, as in many species of *Ixodes*, the male is often not parasitic at all, and may differ markedly from the female in the reduced structure of its hypostome (Fig. 194 *C*, *E* and *F*). In all species the males die shortly after copulation.

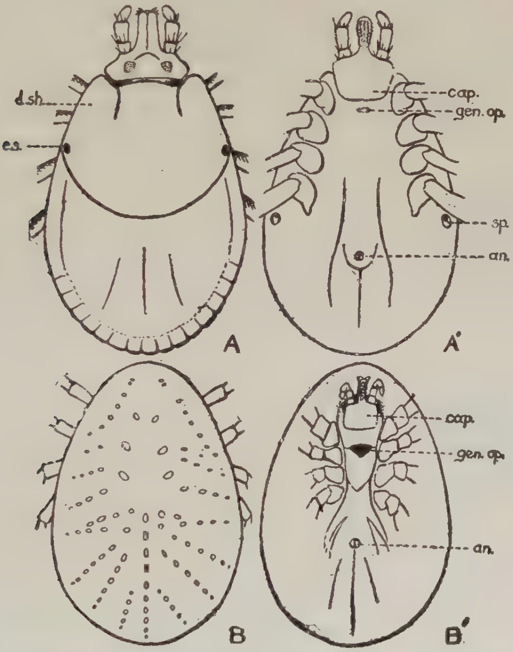

FIG. 196. Comparison of dorsal and ventral view of Ixodid and Argasid females; *A*, dorsal view of Ixodid ♀; *A'*, ventral view of same; *B*, dorsal view of Argasid ♀; *B'*, ventral view of same. *An.*, anus; *cap.*, capitulum; *d. sh.*, dorsal shield; *e. s.*, eye spot; *gen. op.*, genital opening; *sp.*, spiracle.

This, in general, is the life history of ticks, but it is, of course, subject to considerable variation in different species. In many species there are two nymphal periods instead of one. In some species, as in the Texas fever tick, *Boöphilus annulatus*, the moulting takes place directly on the host, thus doing away with the great risk of being unable to find a new host after each successive moult. In a few species the first moult is passed through on the host, but the second is passed on the ground. The most important asset of ticks to counterbalance the disadvantage of having to find new hosts is their extraordinary longevity. Larvæ of ticks have been known to live more than six months without food, and adults have been kept alive in corked vials for five years.

There are two families of ticks, the Argasidæ and the Ixodidæ. The Argasidæ include the bird ticks and their allies, which are distinguished from the Ixodidæ by the absence of a dorsal shield and in having the head partially or entirely concealed under the overlapping anterior margin of the body (Fig. 196). These ticks are chiefly inhabitants of warm countries. Both nymphs and adults feed at night, usually dropping off their hosts immediately after a meal, and thus seldom being carried from the lairs or abodes of their hosts. The Ixodidæ, on the other hand, inhabit the hosts rather than their lairs, and frequently remain attached for several days, or even longer. In the less capacious Argasidæ the females lay their eggs in a number of installments after successive feeds, and the total number of eggs may be counted in hundreds instead of thousands. The reason for this difference is readily accounted for by the difference in habits in the two families, since the progeny of the Argasidæ, reared in the lairs of the hosts, have far better chances of finding a host and of surviving than do the progeny of the Ixodidæ which live on their hosts and may drop off to lay their eggs almost anywhere in the wanderings of the host.

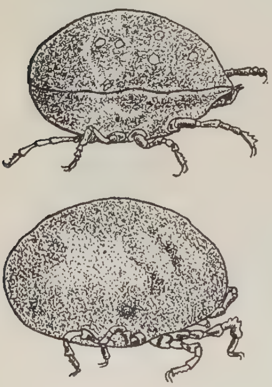

FIG. 197. *Argas* (above) and *Ornithodoros* (below) as they appear when engorged. (After Brumpt.)

Both families of ticks contain some species which are transmitters of human disease and numerous others which are troublesome on account of the painfulness or subsequent effects of their bites. The family Argasidæ contains three genera, *Argas*, *Ornithodoros* and *Otobius*. In *Argas* the body is oval and flattened, with sharply defined margins at the sides, and the head is set well back behind the anterior margin of the body on the ventral side. There are four or five species inhabiting Europe, Persia, East Africa and America, some of which are primarily parasites of birds, others of mammals, but all of them produce painful bites on human beings, and some, especially *A. mianensis*, commonly live and breed like bedbugs in dirty human habitations. In *Ornithodoros* the body has more rounded margins and tends to be pointed in front; the head is very slightly behind the anterior margin on the ventral side. There are numerous species found in the warm parts of America, Asia and Africa, most of them parasitic on mammals and many of them troublesome to man. *Otobius* contains a single species, the ear tick, *O. mégnini*, which has its body covered with short, stiff bristles.

The family Ixodidæ contains 9 genera with numerous species, most of which are parasites of mammals, although some attack birds and reptiles and even amphibians. As a rule these ticks do not prove as great human pests or produce as severe bites as some of the Argasidæ. The principle genera can be distinguished by the characters of the mouthparts as shown in Fig. 198 and by the characters mentioned in the accompanying table.

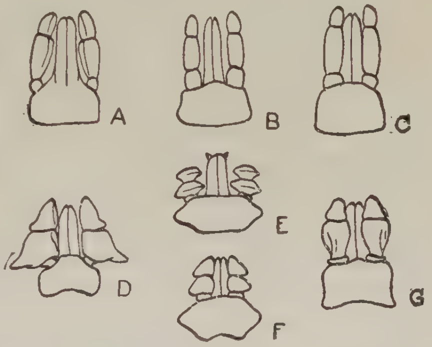

Fig. 198. Diagrams of rostra or capitula of important genera of Ixodid ticks, useful in identification. (After Nuttall.)

With long rostrum

A. *Ixodes*. Anal groove surrounds anus anteriorly, open posteriorly; eyes absent; no festoons.

B. *Hyalomma*. Anal groove postanal; festoons present or absent; male with adanal plates.

C. *Amblyomma*. Anal groove postanal; festoons present; no adanal plates on male.

With short rostrum

D. *Hæmaphysalis*. Festoons present; inornate; eyes absent; no ventral plates.

E. *Boöphilus*. Festoons absent; inornate; adanal and a pair of accessory adanal plates present. *Margaropus* differs in having accessory adanal plates connected with adanal as forked lateral branches.

F. *Rhipicephalus*. Festoons present; usually inornate; ventral plates present in male.

G. *Dermacentor*. Festoons present; ornate; male without ventral plates; basal piece of capitulum rectangular. *Rhipicentor* differs in having basal piece of capitulum hexagonal with prominent lateral angles.

Tick Bites. — The status of ticks as human parasites, as stated before, is one not to be passed over lightly. Aside from the transmission of diseases tick bites are dangerous to man in a number of ways.

The wounds made by ticks, especially if, as sometimes happens, the head is torn off in a forcible removal of the parasite, are very likely to become infected and result in inflamed sores or extensive ulcers, not infrequently ending in blood poisoning. The author, as the result of the bite of a tick in northern California (probably *Dermacentor occidentalis*), suffered from an ulcerating sore on his arm, over half an inch in depth and three-fourths of an inch in diameter. Blood poisoning set in early causing a very high temperature and great pain in the arm, and it was only a timely return to civilization and hospital care that saved his arm if not his life. Sanitary removal of ticks and cleansing of the wounds, as described on p. 438, would be well worth the consideration of every inhabitant or traveller in a tick-infested country.

Tick Paralysis. — More serious than the painful wounds made by ticks is a peculiar paralyzing effect of tick bites, known as tick paralysis. This effect is produced only by rapidly engorging female ticks, especially when attached on the back of the neck or at the base of the skull. There is no evidence of any infective organism being involved although the frequent infections with tularemia of ticks taken from sheep killed by tick paralysis in northwestern United States has led to some suspicion; the paralysis seems rather to be induced by a toxic substance, secreted by the tick while feeding, which has a specific action on the motor nervous system. Either this toxin is only produced during rapid engorgement of female ticks, or is only then injected into the body in such quantity that it cannot be accommodated. Possibly the bite must pierce or come in contact with a nerve or nerve ending in order to produce the effect. The paralysis begins in the legs and usually results in complete loss of their use; the paralysis ascends in the course of two or three days, affecting the arms and finally the thorax and throat. Unless the heart and respiration are affected, recovery follows in from one to six or eight days after removal of the engorging female ticks, even though other ticks remain. If the engorging ticks are not removed, the affection may result in death from paralysis of the heart and respiratory muscles, or in spontaneous recovery after a few days or a week.

Paralysis in man and animals from tick bites has been reported from parts of Oregon and British Columbia in North America, from the island of Crete, from South Africa, and from the east coast of Australia, particularly New South Wales. Fairly numerous cases of tick paralysis occur in children in British Columbia and the Blue Mountains of Eastern Oregon. In this northwest region sheep are especially subject to tick paralysis, to such an extent as to constitute a serious problem in some localities. In this region the spotted fever tick, *Dermacentor* *andersoni*, is the species involved in those cases in which an identification has been made; whether this is because an especially toxic secretion is produced by this tick, or because it more frequently bites along the spinal cord or on the head, is uncertain. Unfortunately in most cases of tick paralysis in children the ticks have not been identified, but there is little reason to doubt that the same tick is usually to blame; it is the only species by the bite of which paralysis has been experimentally reproduced. *Hæmaphysalis cinnabarina* has also been suspected in Canada.

In the island of Crete the species of ticks involved have not been definitely determined but *Hæmaphysalis punctata* and the common European dog tick, *Ixodes ricinus*, are suspected. In South Africa tick paralysis is frequently caused in sheep by the russet tick, *Ixodes pilosus*. On the east coast of Australia another species of *Ixodes*, *I. holocyclus*, the scrub tick, frequently causes paralysis in young stock and in dogs. Actual records of human cases are not numerous, but a number of fatal cases, most of them in young children, have been recorded. The scrub tick is in nature primarily a parasite of marsupials, occurring also on rodents and birds, though it does not appear to be injurious to these hosts. It is, like other species of *Ixodes*, a " three host " species, both the larvæ and the nymphs leaving the host to moult. and then seeking new hosts.

Ticks and Disease

Ticks play an extremely important rôle as transmitters of disease to domestic animals and, fortunately to a somewhat less extent, to man. At least four different types of disease germs are transmitted by ticks, namely spirochætes, Piroplasmidea, Rickettsias and a bacterium, *Pasteurella tularensis*. The list of diseases caused by these organisms and transmitted by ticks is indeed a formidible one. Of spirochætes a number of strains of *Treponema recurrentis*, causing human relapsing fever, are transmitted by various species of *Ornithodoros; T. anserina*, causing a serious disease of chickens, water fowl and other birds, by several species of *Argas* (experimentally also by *Ornithodoros moubata* and chicken mites); and *T. theileri*, a parasite of cattle, sheep, etc., by *Boöphilus* and *Rhipicephalus*. Of Piroplasmidea a number of species of *Babesia* causing Texas or red water or biliary fever are transmitted to cattle and sheep by *Boöphilus* and *Rhipicephalus*, to horses and camels by *Dermacentor reticulatus*, *Rhipicephalus* and probably other ticks, and to dogs by *Rhipicephalus;* and *Theileria parva*, causing African East Coast fever, by *Rhipicephalus* and *Hyalomma*. Of Rickettsia-like organisms *Dermacentroxenus rickettsi*, the cause of spotted fever in man, is transmitted by *Dermacentor andersoni*, and also by other ticks among rodents; and *Rickettsia ruminantium*, the cause of heartwater among ruminants, by *Amblyomma hebræum*. *Pasteurella tularensis*, a bacillus causing tularemia, is transmitted to man by *Dermacentor andersoni*, and among rodents also by *Hæmaphysalis leporis-palustris*. Noguchi has also demonstrated that Oroya fever can be experimentally transmitted by *D. andersoni*.

It has further been demonstrated that *Ornithodoros moubata* may serve as an intermediate host of *Trypanosoma cruzi* and that this parasite may persist in its gut indefinitely in an infective form. There is, however, no evidence that the trypanosome can be naturally transmitted by this or other species of *Ornithodoros*. Experiments to infect *O. moubata* with *Trypanosoma rhodesiense* have failed. On the other hand, surra, a trypanosome disease of horses, camels, etc., has been shown to be transmissible by *Ornithodoros crossi* for several months after an infective feed. Other diseases known or suspected of being transmitted by ticks are louping ill of sheep, of unknown etiology, by *Ixodes ricinus;* Vrijburg's disease of cattle, by unidentified ticks; *Anaplasma* infections in cattle and sheep by *Boöphilus* and *Rhipicephalus; Hepatozoön canis* infection in dogs by swallowing of infected *Rhipicephalus;* and various diseases known as " tick-bite fever " or " tick typhus " by a variety of ticks principally in Asia and Africa.

As can be seen from this list several human diseases are, or can be, transmitted by ticks, the most important ones being relapsing fever and Rocky Mountain spotted fever. Fortunately man is not subject to any Piroplasmid infections, which are such scourges of domestic animals in many parts of the world.

The transmission of Texas fever by ticks is of particular interest because its discovery by Theobald Smith and Kilbourne in 1893 was the first case in which an arthropod was shown to be the intermediate host and transmitter of a protozoan infection. It was five years later that the transmission of malaria by mosquitoes was successfully demonstrated.

The rôle of ticks as carriers of human disease was first established by Dutton and Todd in 1905, when they showed that the African type of relapsing fever was transmitted by the tampan or house tick, *Ornithodoros moubata* (Fig. 155). A year later Ricketts showed that spotted fever in the United States was dependent for transmission upon a tick, *Dermacentor andersoni*. Recently a similar disease, occurring sporadically, has been observed in India and in Nigeria, and on epidemiologic grounds it is believed that it is a tick-borne infection; on account of its similarity to spotted fever and of this disease to typhus, Megaw has suggested the name "tick-typhus" for all tick-borne typhus-like infections, including spotted fever, thus bringing out their relation to louse-typhus and mite-typhus (tsutsugamushi). In recent years tularemia, a disease caused by a bacillus, *Pasteurella tularensis*, allied to the bacillus of plague, has been shown by Parker and Spencer to be transmitted by ticks, and also to be hereditarily transmitted by ticks to their offspring. This is the first known instance of true bacteria being transmitted in this manner.

Ticks and Relapsing Fever. — The fact that tick bites frequently give rise to a serious disease, now known as relapsing fever, has been known in Africa for many years, in fact Livingston in his "Darkest Africa" speaks of this disease as resulting from tick bites. Subsequently it was shown that similar diseases, caused by related if not identical spirochætes, are transmitted by ticks in Persia and in Central and South America, and, more recently, in Spain. The various forms of spirochætes resemble each other very closely morphologically and cannot be differentiated with certainty on morphological grounds, but they differ in immunological reactions. This is likewise true of those forms of the spirochætes which are not transmitted by ticks but by lice. The details of the rôle played by ticks in harboring and transmitting relapsing fever spirochætes and a description of the disease can be found in Chapter IV, pp. 50–57.

The ticks which are implicated in the transmission of relapsing fever in Africa are *Ornithodoros moubata* and *O. savignyi*. The former species, known as the "tampan" or "carapato" is widely distributed in Central Africa from Congo to the East Coast and Madagascar, south to about the 20° parallel, and it appears to transmit relapsing fever wherever it occurs. It appears to be absent north and west of Belgian Congo, where relapsing fever is transmitted by lice. In Abyssinia and through southwestern Asia to India it is replaced by *O. savigni*, which also transmits the *duttoni* strain of relapsing fever. In North Africa and Spain it is replaced by *O. marocanus*, which transmits the *hispanicum* strain of relapsing fever in Spain and Morocco. Another North African species, *O. normandi*, is the transmitting agent of a spirochæte among small rodents (gerbilles).

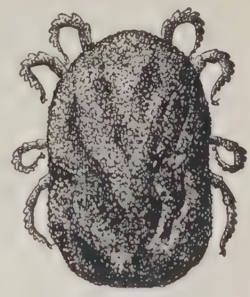

FIG. 199. The tampan, *Ornithodoros moubata*. × 3.

O. moubata is a broad, oval, mud-colored tick (Fig. 199); the females are about 10–14 mm. long and the males only about 6 mm. The hard leathery cuticle is covered with little shiny tubercles and the legs have rounded flattened processes on them which are very characteristic. The adults inhabit the dirty, thatched houses of the natives, where they become great pests. They avoid excessive moisture, and in wet weather leave their hiding places in soil and trash to climb in the crevices of the walls or even in the thatch of the roofs. They occur especially in rest houses along the routes of travel, being readily carried and dispersed in bedding carried by caravans. They have also been found in the burrows of warthogs. They do not remain on the hosts except to feed, which is usually at night; usually they remain attached for from fifteen minutes to an hour or two, engorging until they are distended like cherries (Fig. 197). At the conclusion of each meal the ticks exude an abundant serum-like " coxal fluid " from coxal glands situated between the first and second pairs of legs, after which they retire. This secretion of coxal fluid is important because the fluid contains living spirochætes in infected ticks, and contamination of the wound by this fluid may cause infection. The anal excretion is also said to be infective, but spirochætes have not been observed in it. There is little doubt, however, but that infection frequently results directly from the bites, since spirochætes also occur in the salivary glands.

The females deposit their eggs, totalling from 100 to 300, in batches of 50 or more, depositing them under their bodies in dry soil or trash. The six-legged larvæ develop in about eleven days but, unlike most of the species of *Ornithodoros*, remain without feeding in the egg shell until ready to moult for the first time. At about the time of this moult the egg shell bursts and liberates an eight-legged nymph, generally at the end of about 16 days. The nymphs have excellent appetites and repeatedly engorge themselves at the expense of sleeping human occupants of the houses they infest. The bites are painful, and relapsing fever is as readily transmitted by the nymphs as by the adults. They moult a number of times, gradually increasing in size, and finally become adults. No more moulting occurs after egg-laying begins.

O. savignyi of Abyssinia and southwest Asia is very similar but has eyes, a finer granulation of the cuticle, and larger processes on the legs. It is more diurnal and has more tendency to frequent native bazaars, cattle pens, etc. *O. marocanus* is a smaller species which is frequently found associated with pigs as well as man in North Africa and Spain; it has no eyes, and has the processes on the legs poorly developed. It is very common in the burrows of porcupines, which are thought to be its natural host; many of these ticks from porcupine burrows naturally harbor spirochætes of relapsing fever type.

In Persia and northwest India there are a number of other species, of which *O. tholozani* is said to transmit relapsing fever in Persia, whither the disease is thought to have been introduced from Africa with negro slaves; in Northwest India *O. lahorensis*, which also occurs in Persia and Turkestan, has been suspected, but experimental transmissions with this tick in Baluchistan have failed. The nymphs are common sheep parasites in Central Asia; it is principally the adults which infest human habitations. In tropical America *O. venezuelensis* has been incriminated as a carrier of the *neotropicalis* strain of relapsing fever in Panama and of the *venezuelense* strain in Colombia and Venezuela. This species is smaller and more elongate than *O. moubata;* it has a number of bare ungranulated spots on its back, and very fine granulations. In habits it very closely resembles *O. moubata,* inhabiting the dirty native huts, and feeding on man by preference. In the original experiments on the transmission of relapsing fever by ticks in Panama, Bates, Dunn and St. John recorded *O. talaje* as the transmitter, but Dunn later found that the species they used was really *O. venezuelensis*. Dunn showed that *O. talaje* also becomes infected, but it lives primarily on rats and is only occasionally found in houses, and so is probably not an important vector of relapsing fever, though it may help in keeping up a rat reservoir of the disease.

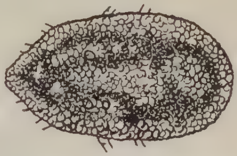

Fig. 200. *Ornithodoros venezuelensis.* (After Brumpt.)

Various other species of *Ornithodoros* occur in the warm parts of America, but have not yet been definitely incriminated as carriers of relapsing fever. *O. turicata* is a very annoying species in Mexico and Central America, living in adobe huts and in pig pens; its bites are so severe that hogs are said to have been killed in a single night by its attacks. Whether or not it can transmit relapsing fever is undetermined. *O. rostratus* of the interior of Brazil apparently does not do so, nor does *O. coriaceus* the "pajaroello" of California and Mexico.

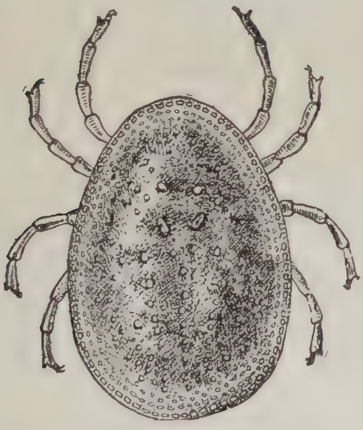

Fig. 201. Persian tick or fowl tick, *Argas persicus.* × 5. (After Braun.)

In all of the proved cases of transmission of human relapsing fever by ticks, species of *Ornithodoros* have been involved, but the Persian "miana" bug, *Argas mianensis,* is suspected of transmission in Persia, though the occurrence there of species of *Ornithodoros* laso, throws some doubt on this. Species of *Argas* (Fig. 201) are the usual transmitters of the relapsing fever of fowls, caused by *Treponema anserinum*, but experimentally *O. moubata* and also chicken mites have been shown to be capable of transmitting this infection. The blood spirochætes of cattle and sheep, on the other hand, are transmitted by Ixodid ticks.

Since the species of *Ornithodoros* have habits almost identical with those of bedbugs, they must be combatted in similar ways. Thorough disinfection by fumigation or by spraying with an insecticide, and scrupulous cleanliness in stalls, coops, kennels, huts or other host homes will effectually eliminate them. Dirty, poorly kept native huts are ideal habitats for these pests. In many parts of Africa infestation is partially prevented by plastering the walls and floors of huts with mud and cow-dung, thus eliminating some of the hiding places; at intervals the huts are smoked out to drive the ticks from the thatched roofs. Travellers who are confronted with the necessity of stopping in infested rest houses can protect themselves by dusting pyrethrum powder between the bed sheets or blankets, or on the mattress. Some protection is also obtained by keeping a light burning beside the bed throughout the night. *O. savignyi*, which often conceals itself to a depth of one inch in dusty soil, can be destroyed in infested camp sites, cattle stalls, etc., by harrowing the surface of the ground, strewing dry grass and brush over it, and burning it from around the edge of the infested area toward the center. Spraying with antiseptics has been found practically useless, since even total immersion of ticks in strong antiseptics for an hour or more fails to kill them.

Ticks and Spotted Fever. — In the case of the Rickettsia diseases, as of the blood spirochætes, ticks share the transmission with lice, but in this case with mites (red-bugs) also. There are three important human typhus-like diseases caused by Rickettsia-like organisms: true typhus, transmitted by lice (as is trench fever, also a Rickettsia disease); tsutsugamushi, transmitted by red-bugs; and spotted fever, as well as sporadic cases of a similar disease referred to in the literature as "tick-typhus," transmitted by ticks.

Spotted fever, discussed more fully on p. 190, is transmitted to man in nature only by the "wood-tick," *Dermacentor andersoni* (formerly *venustus*) (Fig. 202). Experimentally it can be transmitted by other species of ticks, and it is possible that the rabbit tick, *Hæmaphysalis leporis-palustris* may be an important factor in the epidemiology of the disease, as Cooley has pointed out. Thirty per cent or more of infested rabbits have been found to carry infected ticks. For many years spotted fever occurred only in those localities where *Dermacentor* *andersoni* was abundant, since the host relations of this tick, feeding as it does during its early stages of development on the rodents which serve as reservoirs of the disease, and as adults on man, make it preeminently suited for the rôle it plays. There is no evidence that the endemic areas could be rapidly extended by the introduction of a few infected ticks; if this were so the disease would long ago have been far more widespread than it is. Yet in recent years the disease has appeared in widely separated new areas, concomitant with an increase in wood ticks. Cooley believes that the disease already existed in these areas among rabbits and was transmitted by the rabbit tick, which does not bite man. The virus carried by the rabbit tick, as recovered from nature, is very mild in form, and occasional human cases might occur unnoticed. After repeated transmission by wood ticks, which very commonly attack rabbits in their early stages, to a variety of the rodent hosts and then to man, it is quite conceivable that the virulence of the disease might be built up in this manner until it not only could infect man, but could produce increasingly severe disease. Such a stepping up of virulence over a period of years has actually been observed in some localities. The sporadic cases of " tick typhus " which have been reported in India and parts of Africa may likewise indicate a disease already prevalent among rodents or other native animals, and only occasionally transmitted to man, either on account of reluctance on the part of the transmitting ticks to bite man, or of insusceptibility of man to most strains of the parasite.

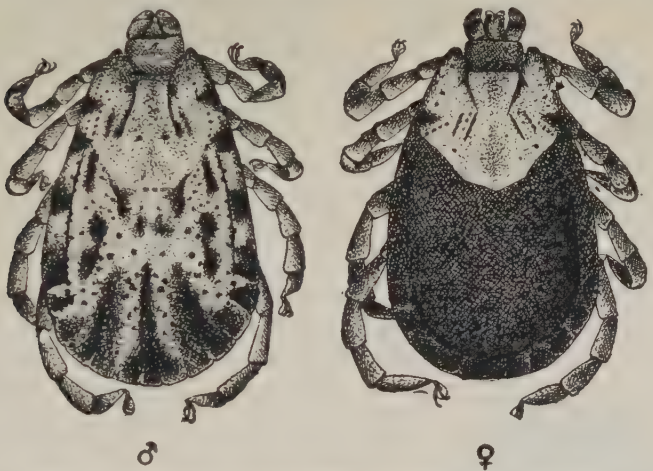

FIG. 202. Spotted fever tick, *Dermacentor andersoni*, male (♂) and female (♀). × 12.

Dermacentor andersoni is a handsome reddish brown species, the male of which has the whole back marked with black and silvery-white lines, while the female has only the small dorsal shield marked with silver, the abdomen being deep reddish brown. This species is one which requires two different kinds of hosts to complete the life cycle. The six-legged larvæ (Fig. 203*B*), of which there are about 5000 in a brood, attach themselves to any of the rodents which abound in the country where the ticks occur, especially squirrels of various kinds. Usually the larvæ, and the nymphs also, attach themselves about the head and ears of their host. After a few days the larvæ drop, transform into nymphs (Fig. 203*C*) and again attack their rodent hosts. After dropping off these and transforming into adults they no longer pay any attention to the rodents but seek larger animals, especially preferring horses and cattle, though they readily attack other large wild and domestic animals and man. Their original wild hosts were probably the mountain goats, elk and other wild game of the region, but with the supplanting of these by domestic animals the latter have become the main host animals of the ticks. Unlike most ticks, this species may take two or even two and a half years to complete its life cycle under unfavorable conditions. The winter is passed in either the nymphal or adult stages.

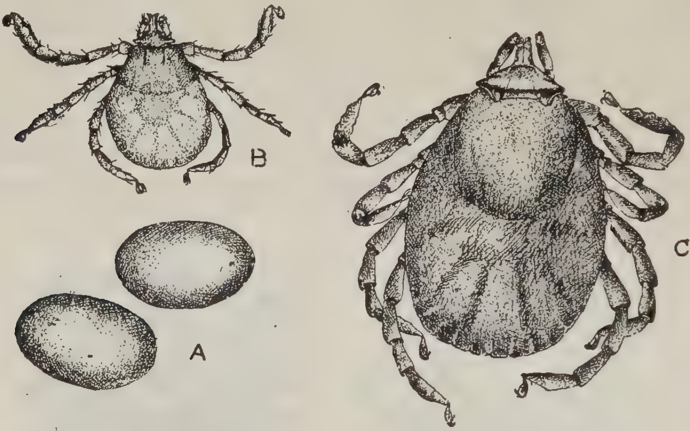

Fig. 203. Development of spotted fever tick, *Dermacentor andersoni; A*, eggs; *B*, larva; *C*, nymph. × 30.

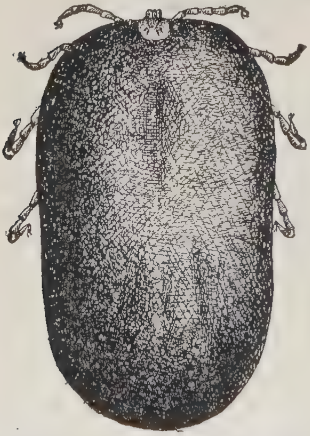

Fig. 204. Spotted fever tick, *Dermacentor andersoni;* engorged female. × 4.

Dermacentor andersoni is found in a limited area in northwestern United States and British Columbia, east to eastern Montana and eastern Wyoming, west to the Cascade Mountains and south into Nevada and Colorado. This distribution somewhat exceeds the present distribution of spotted fever.

The rabbit tick, which as already shown may perhaps keep up a spotted fever infection in rabbits even in places where no human spotted fever occurs, is a large, very dark-colored species which is rarely found except on the ears of rabbits or heads of birds. It can play no part in human infection. West of the Cascade and Sierra Mts. in Oregon and California, however, there occurs another species of *Dermacentor*, *D. occidentalis*, which in the adult stage frequently attacks man, though its normal hosts are probably deer and other large ungulates; in its earlier stages it will readily engorge on rodents though it is uncertain to what extent it does so in nature. There is a possibility that if spotted fever became endemic among rodents within its geographic range, this species might frequently transmit it to man. Occasional transmission to man would also be expected from other ticks in other parts of America if the disease were introduced and established among rodents. *Dermacentor variabilis*, a widely distributed American dog tick, might very easily play an important rôle in this case, since its nymphs are commonly found on squirrels. The carrying of infected ticks on animals shipped from the infected areas to other parts of the country constitutes a distinct danger.

Control and eradication of the spotted fever tick, in view of its wide variety of hosts, has proved a very difficult and important problem. Not only is it at present the sole means of dissemination of spotted fever in man, but it also frequently causes tick paralysis in children and may cause heavy losses of sheep from this cause; it is an important factor in the transmission of tularemia among rodents and occasionally to man; and it causes much discomfort and often severe ulcers in man and domestic animals by its bites. One of the most important control measures is rodent destruction, since in this way not only are the hosts of the early stages of the tick eliminated, but the rodent reservoir of spotted fever is reduced. In Montana special efforts are directed against the ground squirrels which are the most abundant hosts for the immature ticks and, unfortunately, the most difficult to exterminate; woodchucks, rabbits and chipmunks are of somewhat less importance. Additional measures consist in the dipping or hand picking of domestic animals, in the clearing away of brush and burning over of tick-infested lands, and the systematic grazing of sheep on the infested ranges. The sheep serve as traps for large number of ticks which become entangled in their wool and are starved, although the ticks even the score to some extent by destruction of many sheep by paralysis. In one instance 500 sheep were found to destroy 25,000 ticks in a season.

Another method of control which is still in the experimental stage is the use of minute Hymenopteran insects of the genus *Ixodiphagus* which parasitize the nymphs of many kinds of ticks, and seem to attack *Dermacentor andersoni* especially readily. It is said that ticks have been practically exterminated in parts of France where one of these parasites is present.

Ticks and Tularemia. — Tularemia was first described in 1910 by McCoy as a plague-like disease of ground squirrels in California, caused by a bacillus, *Pasteurella tularensis*, which is closely related to the organism causing plague. It has subsequently been extensively investigated by Francis and others, and is now known to be a wide-spread infection endemic among rodents, particularly ground squirrels and rabbits, in many parts of the United States and also in Japan. It is perpetuated among rodents by blood-sucking arthropods, and causes sporadic infections among other animals which feed on rodents, and frequently in man, sometimes as the result of handling infected animals, sometimes from the bites of the arthropod transmitters. Many different arthropods, including deerflies, lice, fleas and ticks have been shown to transmit the infection experimentally, but in nature the disease is most commonly transmitted by ticks from rodent to rodent, and by ticks or deerflies to man. The ticks known to be involved are *Dermacentor andersoni* and *Hœmaphysalis leporis-palustris*, although only the former is responsible for human cases. While the deerflies are purely mechanical transmitters and capable of causing infection only by their bites and at most for only four days, the ticks acquire a general infection of intestine, feces, epithelial cells of the gut, and body cavity. The bacteria survive the winter in ticks, are carried over from one stage of development to another, and are even transmitted through the eggs to the offspring. The ticks probably infect both by their bites and by contamination of the bites with the feces. Merely handling an infected tick may result in infection: thus in one instance a man pulled a tick from his horse and then removed a foreign body which had blown in his eye; two days later the eye became inflamed, the lymph glands on that side of his head became enlarged, and he developed a typical case of tularemia.

In the northwestern part of the country, especially in Montana, where *Dermacentor andersoni* is abundant, tularemia frequently causes great epizoötics among jack rabbits, and a high mortality results, often accompanied by epidemics of human cases. As in the case of spotted fever, it is evident that the disease would be much more frequent in man in other parts of the country if there were as efficient go-betweens between rodents and man. In Washington, D.C., seven of 914 rabbits examined in the market contained virulent *Pasteurella tularensis*, and seventeen human cases occurred from dressing rabbits in that market, yet no human cases have been reported in that part of the country from insect or tick transmitters. The rôle of deerflies in transmitting tularemia is discussed further on p. 530.

There are also some suggestive facts in connection with the occurrence of tularemia infection in ticks which have been removed from sheep which have died from supposed tick paralysis. The possibility has been considered that at least some of the cases of tick paralysis in sheep may actually have been due to tularemia, but the present evidence is against the identity of these two pathological conditions.

Other Troublesome Ticks

Many of the most important ticks attacking human beings have been discussed in connection with the transmission of disease. Some of the species of *Ornithodoros* are probably the only ticks which can be considered as primarily human parasites, since they normally infest human habitations, but even many of these, including some that serve as transmitters of relapsing fever, are at least as frequently parasites of other animals, such as pigs, cattle, sheep, rodents, etc. There are, however, many other ticks which attack man frequently enough, and cause enough annoyance and injury, to be regarded as important human pests. Among the Argasidæ, in addition to those which have been discussed in connection with the transmission of relapsing fever, should be mentioned the several species of *Argas*, and also the Californian *Ornithodoros coriaceus.* Of the latter, known as the " pajaroello," Herms states that " natives, principally Mexicans, in the vicinity of Mt. Hamilton fear this parasite more than they do the rattlesnake, and tell weird tales of this or that man having lost an arm or leg, and in one instance even death having ensued, as a result of a bite by the Pajaroello. There seems to be a suspicion in that region that three bites will result in certain death. The stories all agree in the essential detail that the bite results in an irritating lesion which is slow to heal and often leaves an ugly deep scar." The tick is about two-fifths of an inch in length, irregularly oval, with thick turned-up margins, roughly shagreened, and of a yellowish earthy color spotted rusty red. It occurs in the Coast Range mountains of California and in Mexico and according to Herms is most commonly found in the dry leaves under live-oak trees where cattle or other animals are accustomed to lie in the shade. It passes through from four to seven moults to reach the adult state, occupying from one to two years to complete its life history, according to its success in finding suitable hosts. The bites of this tick produce sharp pain, accompanied by a considerable discoloration around the wound, and if on an arm or leg the whole limb may become greatly swollen as in the case of a snake bite. After scabbing over, the wound may continue to exude lymph and to be irritable for several weeks, and it is possible that infection and consequent blood-poisoning might readily occur, thus giving a basis for the tales mentioned above.

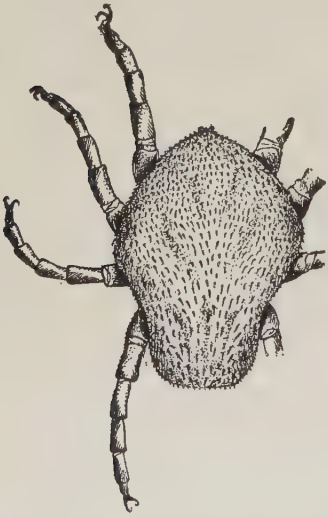

Fig. 205. Spiny nymph of ear tick, *Otobius* (or *Ornithodoros*) *mégnini*. × 10. (After Marx from Banks.)

Another noteworthy member of the Argasidæ is the spinose ear tick, *Otobius* (or *Ornithodoros*) *mégnini* (Fig. 205), of southwestern United States and Mexico, and now becoming common in parts of South Africa. It is very troublesome to man as well as to horses and other domestic animals. The nymphs, which develop from the larvæ in the ears of their hosts, are peculiar in having very spiny bodies, quite different from the smooth larvæ and adults. The nymphs may remain attached to their hosts for months but finally drop off to transform into adults. In nature they probably often leave their hosts at night as do other Argasidæ. The adults are not parasitic but lay their eggs without further feeding. The pain and annoyance caused by the spiny nymphs in the ears of domestic animals is sufficient to cause the animals to become ill-tempered and emaciated. Children sometimes suffer a great deal from their attacks, and have difficulty in dislodging the invaders from their ears. This can readily be done, however, by pouring olive oil or some other harmless oil into the ears.

A mixture of pine tar (2 parts) and cottonseed oil (1 part) is recommended for killing these ticks in the ears of domestic animals.

Some of the species of *Argas*, most of which are primarily bird parasites, often annoy people who come in contact with infested chicken coops or pigeon cotes. One species, *A. mianensis*, found in Persia and long confused with the fowl tick, *A. persicus*, lives and breeds in the dirty huts occupied by the natives, and is a great tormentor of the inhabitants; the bites often result in fever and constitutional disturbance, but whether merely as the result of the poisonous bite or due to disease organisms inoculated is unknown. This species has also been suspected of transmitting relapsing fever.

Of the family Ixodidæ there are numerous species which occasionally attack man, but few habitually do so. Only a few species need special mention here. *Dermacentor andersoni* is of preëminent importance on account of its rôle in the transmission of spotted fever and tularemia, but it and *D. occidentalis* both very commonly attack man, and their bites are particularly likely to cause ugly ulcerating sores. *D. variabilis*, the American dog tick, is a hardly less frequent human pest. A particularly obnoxious species in tropical America is *Amblyomma cajennense* which not only is a very frequent and annoying pest in all stages of its development, but according to observations made by Dunn in Panama, its bites are frequently infected by *Dermatobia* larvæ. The evidence seems conclusive that this tick not only acts as a carrier of the eggs of this fly but is also instrumental in assisting the larvæ to penetrate the skin. This Cayenne tick is also suspected of transmitting the forest leishmaniasis of South America (see p. 134), and the fact that it can harbor leprosy bacilli for at least 13 days leads to speculation as to a possible even more sinister rôle. Another *Amblyomma*, *A. maculatum*, is a widely distributed human pest in the warm parts of America; it has been used in place of medicinal leeches by primitive peoples. *A. americanum* has been reported by Spencer as causing a case of typhus-like fever in Virginia.

In the Old World the European dog tick, *Ixodes ricinus* and also *I. putus* are widely distributed species which are not averse to human blood. In South Africa two other species, the russet tick, *Ixodes pilosus*, and the bont tick, *Amblyomma hebræum*, are important. The former species is associated with tick paralysis, whereas the larvæ of the latter produce itching and painful wounds which may be followed in a week or so by fever, headache, skin eruptions and other symptoms. The name " tick-bite fever " has been applied to this malady, which is perhaps a form of " tick-typhus " such as occurs sporadically in India, Malaya and Nigeria, and is believed to be related to spotted fever. The disease caused by bont ticks is followed by immunity to subsequent attacks, so that usually only new arrivals are affected. *Rhipicephalus simus* is also incriminated as a cause of "tick-bite fever" in South Africa. *R. sanguineus* is the suspected cause of " tick typhus " in India. In Australia *Ixodes holocyclus* is one of the commonest human biters, and is of importance on account of its causation of tick paralysis.

Treatment and Prevention. — As shown above tick bites may be attended by a number of serious results, such as fever, ulcerating sores, paralysis or disease transmission. The treatment of the bites, therefore, may be of considerable importance. It has been shown that ticks, at least in the case of the relapsing fevers, do not ordinarily infect directly by biting, but by contaminating the wound with infected coxal fluid or excrement. It is obvious, therefore, that disinfection of the wound after removal of the tick would be a precaution of great value in places where ticks carry diseases to which human beings are susceptible. Such treatment would also prevent bacterial infections of various kinds from entering the wounds and causing ulceration or blood-poisoning.

Ticks should never be removed forcibly since if so handled the head may tear off from the body and remain in the wound, held there by the ugly barbed proboscis. A drop of kerosene, creoline or some other oil on the head of the tick will cause it to withdraw its beak and drop off in the course of a minute or two. A greasing with lard or vaseline to close up the spiracles accomplishes the same thing. Disinfection of the wound with iodine, alcohol, lysol or other disinfecting agent should follow immediately.

Precautions against tick bites where serious diseases are likely to result are of the greatest importance but very difficult. King, while investigating spotted fever, spent a whole season in the heart of the Bitter Root Valley in Montana where spotted fever infection was most dangerous. He wore high-topped shoes and cotton outer garments soaked in kerosene and had pieces of khaki cloth soaked in kerosene sewed to the tops of his boots or fastened by drawstrings higher up on his leg. A leg covering of oil-proof material with crude oil applied on the outside would be of benefit, according to King. A vaccine against spotted fever is, however, now available. In Abyssinia the attacks of *Ornithodoros savignyi* are prevented by rubbing the feet with turpentine.

Means of control of tick pests vary considerably with the different species, depending on the hosts, their seasonal history, their varying life histories and other factors. Some of the special control measures against *Ornithodoros* and *Dermacentor andersoni* have already been discussed.

Most of the species of ticks which attack man are normally parasitic on domestic animals, and therefore means of exterminating ticks on the latter would tend to reduce the human pests.

Ticks on domestic animals may be destroyed either by hand treatment or by dipping, or by the elimination of ticks from pastures by starvation. The cattle tick, *Boöphilus annulatus*, has been eliminated from many ranches by a skillful manœuvering of the cattle, driving them from field to field in such a way that in the course of a number of months the ticks would all have dropped and perished from starvation. Such a plan is not feasible for many species since a variety of hosts may be utilized, and long periods of starvation can be endured without injury.

Dipping of infested animals is a good control method. An arsenical dip has been found best adapted for destruction of ticks on their hosts, a description of which, with methods of preparing and using, is given in Farmers' Bulletin No. 378 of the U. S. Department of Agriculture. A brief but thorough immersion in an arsenical dip kills ticks as effectively as a long one. The deeper skin cells of host animals seem to have an affinity for arsenic and store it up; this arsenic is believed to be ingested subsequently by the ticks with blood or lymph passing through the arsenic-laden skin layers.

Hand treatment with arsenical dip by means of rags, mops or sprays is sometimes found more practical but is usually less thorough.

Another suggested control measure is the use of " molasses grass," *Melinis minutiflora*, as a forage grass. It has a strong odor which is believed to act as a repellent, and ticks are said not only to be absent from pastures covered with it, but also to stay off cattle which have recently fed on it. In Colombia it is said that the *Dermatobia* fly is also disappearing before the extending cultivation of this grass. It affords, however, rather poor forage, and is therefore to be looked upon only as a last resort. It could, however, be effectively used for bedding for poultry and animals, as indeed it has been in some parts of Africa.

Natural enemies, particularly such birds as starlings and egrets, play a considerable part in tick control in some localities. In many parts of India cattle are constantly attended by white egrets or " paddy birds," each animal being escorted while grazing by one or more of the white-uniformed attendants, which can frequently be seen perched on the animals busily picking off ticks.

Control measures againt the Argasid ticks which infest the homes and lairs of their hosts, attacking only at night and for brief periods, are somewhat easier, and are similar to control methods against bedbugs. They have been discussed on p. 430.

CHAPTER XXIII

BEDBUGS AND THEIR ALLIES

The Order Hemiptera. — The order of insects, Hemiptera, which includes the true bugs, contains numerous species, many of them aquatic, most of which are predaceous or feed on plant juices, but there are some which habitually or occasionally suck blood. The most important of these are the bedbugs, which are found all over the world in temperate and tropical climates. There are few objects which are more disgusting than bedbugs to good housekeepers, yet there are few who, at one time or another, have not had to contend with them or at least guard against them. Belonging to an allied family are the cone-noses, larger than bedbugs and not devoid of wings, fiercer in disposition and some of them capable of producing much more painful bites. A considerable number of species of these bugs are known and are found in all warm countries. The relation of bugs to disease is still very imperfectly known, but these insects are positively known to be the principal transmitters of at least one important disease, and are suspected of transmitting several others.

The true bugs have an incomplete metamorphosis, the adult condition being attained gradually by successive moults of the nymphs (see p. 391). They have piercing and sucking mouthparts enclosed in a jointed beak, and even many of the plant-feeding forms are capable of inflicting painful wounds. The wings, except in those forms, like the bedbugs, in which they are vestigial, are very characteristic; the first pair, called hemelytra, have the basal portion thickened and leathery while the terminal portion, which is sharply demarcated, is membranous (Fig. 206). The second pair of wings are membranous and folded in plaits when at rest. Many bugs have "stink-glands" between the bases of the hind legs which secrete a clear volatile fluid by means of which they emit a strong offensive odor.

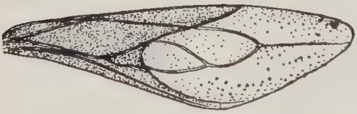

FIG. 206. A hemipteran wing (Reduviid).

Bedbugs

General Account. — The bedbugs belong to the family Cimicidæ. They have broad, flat reddish-brown bodies, and are devoid of wings, except for a pair of spiny pads which represent the first pair of wings

(Fig. 207). In the male the abdomen is quite pointed at the tip, whereas in the female it is evenly rounded, the contour of the abdomen being almost a perfect circle in unfed bugs. The eyes project prominently at the sides of the head, the flexible four-jointed antennæ are constantly moved about in front of the head, and the three-jointed beak is folded under the head so that it is entirely invisible from above. The legs have the usual segments, the tarsi being three-jointed. The greater part of the body is covered with bristles set in little cup-shaped depressions. These depressions are perforated at the bottom to allow for the passage of muscles which move the bristles. Murray describes having seen bugs raise the bristles upon meeting each other as cats raise their hairs or birds their feathers. The bristles are of two kinds, one a simple slender spine, the other with a stouter flattened end, with sawlike teeth along the thinner edge. In addition to both kinds of bristles, the legs also have a dense brush of hairs at the end of each tibia. When a bug is distended with blood a smooth shining band can be seen at the base of each abdominal segment where no bristles occur (Fig. 207). These bands are the portions of the segments which are not ordinarily exposed, being overlapped by the preceding segment.

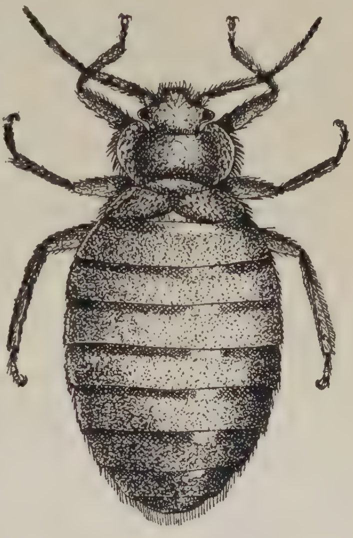

FIG. 207. Bedbug, *Cimex lectularius*, female. × 10.

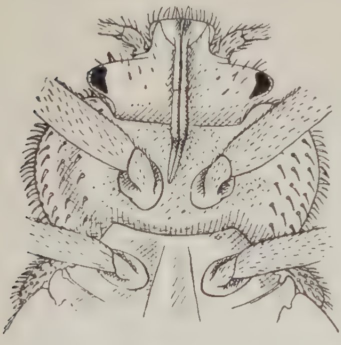

FIG. 208. Head and part of thorax of bedbug, ventral view. × 20. Note jointed beak, eyes and stout spines.

One of the most striking characteristics of bedbugs is the peculiar pungent odor so well known to all who have had to contend with these pests. As in other bugs the adults have the stink-glands situated in the last segment of the thorax and opening by a pair of ducts between the coxæ of the hind legs. In the first four nymphal stages these glands are not present, but are replaced by glands situated on the dorsal side of three of the anterior abdominal segments. Although in most "wild" bugs the stink-glands are supposed to be distinctly beneficial in that they make the owners obnoxious to enemies which would otherwise prey upon them, they are a decided handicap to the domestic bedbugs in the struggle for existence, since the odor draws attention to the presence of bugs which might otherwise escape notice. Nor does the scent appear to be any protection to them against such enemies as cockroaches and red ants. Murray suggests that it may be of some use to them in their social intercourse in the dark recesses in which they spend their lives.

The nasty odor of bedbugs has evidently inspired some faith in their medicinal value. Seven bugs ground up in water was said by Pliny to arouse one from a fainting spell, and one a day would render hens immune to snake bites. Even at the present time there are places in civilized countries where bedbugs are given as an antidote for fever and ague.

The true bedbugs belong to the genus *Cimex*, but not all the species are human parasites; some confine their attentions, ordinarily at least, to birds and others to bats. There are two widely distributed species which attack man: one is the common bedbug, *Cimex lectularius*, found in all temperate climates and sometimes also in tropical ones; the other is the tropical or Indian bedbug, *Cimex hemipterus* (formerly *rotundatus*) which is the prevalent species in the tropical parts of the world. These two species differ only in minor details. *Cimex hemipterus* is most easily distinguished by the fact that the prothorax is smaller and rounded to the margin on the dorsal side, whereas in *lectularius* its lateral portions are flattened expansions (cf. Figs. 207 and 209); it has a much less pronounced odor, and is less dependent on human blood than is its relative of temperate climates, and will attack not only rats and mice but also bats and birds. Brumpt has described another bug, *Cimex* (or *Leptocimex*) *boueti*, as a human parasite in French Guinea; this species has longer legs, fewer bristles, ovoid body, and small rectangular prothorax.

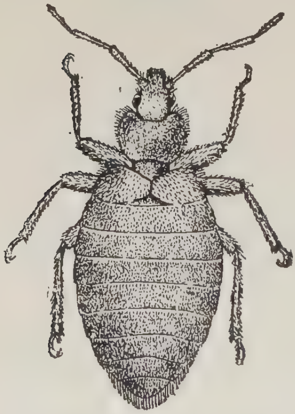

Fig. 209. Indian bedbug, *Cimex hemipterus* (*rotundatus*), female. × 8. (After Castellani and Chalmers.)

Some of the Cimicidæ which do not normally live at the expense of human beings may become nuisances under special conditions. The proverbially super-clean housekeepers of Holland villages, for instance are sometimes greatly chagrined to find bugs in their spotless houses, the bugs being *Cimex columbarius* derived from pigeons nesting in the roofs. Similar temporary invasions by *C. pipistrelli* of bats sometimes occur in dwelling houses, especially when the bats are driven away or migrate, but the widespread notion that bats bring bedbugs into houses is a misapprehension. The assertion that bedbugs can be found under bark and moss out of doors is also erroneous; these bugs are really the immature stages of other bugs, and they only superficially resemble bedbugs. The Mexican poultry bug, *Hœmatosiphon inodorus*, is a related species, resembling a bedbug but having longer legs, no odor, and a very long beak which reaches to the hind coxæ. It is often a serious poultry pest in the dry parts of the Southwest, and sometimes invades houses and becomes an unbearable tormentor of man. The Mexicans frequently abandon or burn their huts to escape from them.

Habits. — Bedbugs are normally night prowlers, and exhibit a considerable degree of cleverness in hiding away in cracks and crevices during the daytime. When hungry they will frequently come forth in a lighted room at night, and have even been known to feed in broad daylight. Favorite hiding places are in old-fashioned wooden bedsteads, in the crevices between boards, under wall paper, and other similar places, for which their flat bodies are eminently adapted. Like other animals which have long been associated with man, bedbugs have developed much cunning in their ability to adapt themselves to his habits. Marlatt says " the inherited experience of many centuries of companionship with man, during which the bedbug has always found its host an active enemy, has resulted in a knowledge of the habits of the human animal and a facility of concealment, particularly as evidenced by its abandoning beds and often going to distant quarters for protection and hiding during daylight, which indicate considerable apparent intelligence." Their ability to gain access to sleepers at night is hardly less remarkable. Cases are reported of bedbugs creeping along ceilings and dropping down on beds in order to reach their hosts, but these may have been accidental.

The bedbug makes himself a great pest wherever he occurs by the unsparing use of his piercing and sucking mouthparts. The latter consists of four piercing stylets which lie in a groove in the long, jointed lower lip or beak. The outer pair, the mandibles, are slender needle-like organs armed with a row of teeth near their tips, which serve to pierce and lacerate the wound; the inner pair, the maxillæ, are much stouter and longer, grooved on the inner face so that by their apposition they form two canals, one large one for sucking up blood, and one much smaller one for injecting saliva; the two maxillæ are firmly held together by an interlocking device. The groove of the sheath-like lower lip has its margins almost closed together, thus effectually protecting the stilettos inside. When about to indulge in a meal the beak is bent back, and the piercing organs, gliding up and down past each other, are sunk into the flesh of the victim (Fig. 210). A strong sucking motion of the pharynx, into which a bit of salivary juice has already been pumped, draws blood up through the maxillary tube, through a thickened "bottle neck" ring to the esophagus and then into the relatively enormous stomach. The muscles for dilating the pharynx in order to make a suction pump out of it occupy the greater part of the head. According to Cragg, there are about 70 pulsations of the pharynx per minute in young bugs, in which this can be observed through the body wall. Bugs seldom cling to the skin while sucking, preferring to remain on the clothing. Since a fresh meal apparently acts as a stimulus for emptying the contents of the rectum, the adherence to the clothing is a fortunate circumstance, inasmuch as it precludes to some extent the danger of bedbugs infecting their wounds with excrement, as do ticks.

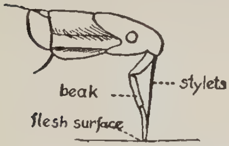

Fig. 210. Diagram showing bug in act of biting. Note bowing back of proboscis. (After Murray.)

In the course of 10 or 15 minutes a full meal is obtained and the bug, no longer flat but round and distended with blood, retreats to his hiding place, having first deposited a bit of excrement. According to Cragg, in the case of *C. hemipterus* (*rotundatus*) a single meal, much of which is temporarily stored in the stomach which acts as a food reservoir as well as a digestive organ, is not fully assimilated for at least a week, although the bug is ready to feed again in a day or two, thus having parts of several meals in the stomach at once. This is quite a different condition from that found in most blood-sucking insects, where a meal is completely digested before another is sought. Observations made by several authors on *C. lectularius* do not indicate that this species has similar habits. As in other bugs, the digestive juices change the absorbed blood into a dense black mass, described by Murray as almost like lamp-black.

The bite of the bedbug seldom produces pain or swelling unless rubbed or scratched, a fact which indicates either that the saliva is not irritating or that it does not ordinarily reach the wound before sucking begins. In some people, however, a stinging, hard, white swelling is produced.

Under normal conditions the common bedbug, *C. lectularius*, has only rarely been found feeding on anything but human blood, but it is able to subsist on the blood of such animals as rats, mice, rabbits, cats, dogs and even chickens. It has also been shown that bugs will suck blood from freshly killed mice. By utilizing mice and rats as a food supply they are able to exist in deserted buildings for a long time. Furthermore they are able to endure long fasts; they have been kept alive without any food whatever for a year. Murray has found that bugs which have been starved even for a long time pass unaltered blood corpuscles in their feces, and suggests that a small quantity of food may be retained undigested in the rectum to be drawn upon very slowly in time of need, though when a fresh supply of blood is obtained the old store is cleared out. Bugs also store up a great deal of fat for use in time of famine. Sometimes, however, after a house has been deserted for some time, and their normal supply of food is cut off, the bugs migrate in search of an inhabited house. In cold weather bugs hibernate in a semi-torpid condition and do not feed, but in warm climates they are active the year around. The common bedbug, according to Marlatt, is sensitive to temperatures of 96° F. to 100° F. or more if accompanied by a high degree of humidity, and is killed in large numbers under such climatic conditions. According to Bacot, unfed newly hatched bugs are able to withstand cold between 28° F. and 32° F. for as much as 18 days, though they are destroyed by exposure to damp cold after a full meal.

Life History. — The eggs of bedbugs (Fig. 211*A*) are pearly white oval objects, furnished with a little cap at one end which is bent to one side. As in the case of lice, the eggs are relatively large, being about one mm. in length, and are therefore laid singly or in small batches. The ovaries hold about 40 eggs at a time, all near the same stage of development, so they must undergo rapid increase in size shortly before being deposited. Girault, who has carried out extensive breeding experiments, saw one female lay 111 eggs during the 61 days that he had her in captivity, and another laid a total of 190 eggs. Often a female returns to lay more eggs in the same place so that batches of 40 or more can be found in the crevices where the insects hide, though smaller clusters are more common.

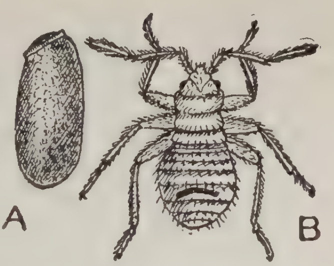

FIG. 211. Egg and newly hatched larva of bedbug. × 20. (After Marlatt.)

The eggs hatch in from six to ten days during warm weather, but are retarded in their development by cold. A week of freezing temperature reduces the hatching to 25%. The freshly hatched bugs (Fig. 211*B*) are very small, delicate and pale in color. After their first hearty meal they have a much more robust appearance, and grow rapidly. The skin is normally moulted five times before the final adult stage is reached, at least one gluttonous feed being necessary before each moult in order to insure normal development and reproduction. Although apparently not necessary to its development, the bug may gorge itself several times between moults, at intervals of about one to six days. Marlatt found the average period of time between moults to be eight days. Allowing a similar length of time for the hatching of the eggs, the time occupied from laying of the eggs to maturity is about seven weeks. Girault has found the development from the hatching of the eggs to maturity to take place in as short a time as 29 days. On the other hand, starvation, cool temperatures and possibly other conditions may drag out the period of development to great length. Bacot found that the newly hatched nymphs could live unfed four and a half months and with one feed for nine months. The several nymphal stages of the insect resemble each other quite closely except in the constantly increasing size and deepening color. The wing pads appear only after the last moult.

Bedbugs and Disease. — The bedbug would appear at first sight to be eminently adapted for human disease transmission. Like an ex-criminal, the bedbug is under constant suspicion; with or without reason it has been on trial in connection with kala-azar and other forms of leishmaniasis, relapsing fever, infectious jaundice, South American trypanosomiasis, leprosy, plague, typhoid, infantile paralysis, some filaria infections, seven-day fever, typhus, tularemia, and even malaria and beri-beri. Yet there is still to be produced any single instance in which the bedbug has been shown to be more than a relatively unimportant accessory in the transmission of any human disease. A recent dispatch from Brazil states that the bedbug has been found capable of transmitting yellow fever to monkeys, but the epidemiology of yellow fever does not favor the view that the bug can be an important factor.

In view of the numerous disease organisms which not only survive but also multiply in the bodies of bedbugs, it is evident that the salivary glands do not become infected as readily as they do in many other insects. Of the numerous pathogenic organisms mentioned above, none except infectious jaundice (from guinea pig to guinea pig) has been shown to be transmitted by the bites, although a number of them can be transmitted by inoculation of crushed bedbugs, or by the feces. Another factor which limits the effectiveness of bedbugs as disease transmitters is their non-migratory habit. Although frequently carried about in clothing they normally live in the homes and not on the persons of their hosts, and they would therefore usually be limited in the spread of a disease to the occupants of the infested place; only an occasional individual is transferred to a new place. In the case of bugs in private homes, any disease transmitted by them would be largely limited to a single family, but in the case of infested hotels, rooming houses, sleeping cars, boats, etc., conditions are ideal for the spread of disease by bugs.

One of the first accusations against the bedbug as a disease vector was made by Patton in India in 1907; he observed that bugs (*C. hemipterus*) fed on kala-azar patients sometimes became infected and that the parasites underwent developmental stages in the gut of the bug similar to the development in culture (see p. 126 for further details). Subsequent investigations by Cornwall showed that infection of bugs fed on kala-azar cases is rare, and that no intracellular phase of development of the parasites occurs in the guts of the bugs, although both flagellated and non-flagellated forms may become extremely abundant in the lumen of the mid-gut. Numerous attempts to transmit the disease experimentally by either the bites or the feces of bugs fed on kala-azar cases have uniformly failed. Cornwall's final conclusion was that the bedbug was not the normal intermediate host but only a casual one in which the parasites could multiply in the flagellated stage as they do in cultures; he suggested that the bedbug be given a rest in connection with kala-azar and other insects be investigated. Later Shortt *et al.* showed that the behavior of *Leishmania donovani* in *C. lectularius* and *C. hemipterus* is different. In the latter species multiplication of the parasites is much less pronounced, passage to the hind part of the mid-gut is more rapid, and disappearance of the flagellates occurs more quickly, usually within two weeks and in most cases in a few days. *C. lectularius* would, therefore, appear to be a better host than *C. hemipterus*, yet it is only the latter species which occurs in the highly endemic areas of Assam. Although, as Napier has pointed out, a few epidemiological facts, such as the house and site nature of the infection and the continued persistence of infectivity in these places even after desertion, and the common occurrence of the disease among the class of people who always have bugs in their houses, would favor the bug transmission hypothesis, the facts of distribution relative to climatic conditions, elevation, vegetation, ground-floor limitation, and rural and urban conditions make it evident that the bug cannot possibly play an important rôle in the transmission of the disease. In occasional instances it is possible that the bedbug might cause infection through the agency of its feces or a soiled proboscis, but such instances appear to be exceptional if they occur at all.

What has been said about the relation of bugs to *Leishmania donovani* of kala-azar is equally true of *Leishmania tropica* of Oriental sore. Although the parasites develop readily in bugs, there is no experimental or epidemiological evidence that bugs are more than at most exceptional transmitters of the infection. There seems to be no specificity in the relation between bugs and the various forms of *Leishmania* or *Herpetomonas;* even *Herpetomonas ctenocephali* of fleas develops readily in their guts.

The relation of bedbugs to the transmission of *Trypanosoma cruzi* is of the same nature. According to Brumpt these trypanosomes developed in about 80% of both *Cimex lectularius* and *C. hemipterus* fed on infected mice, but injections of infected feces produced very slight infections in other mice. As a rule bedbugs remain infected for a much shorter time than do the bugs of the genus *Triatoma,* but may retain the trypanosomes for several months. Parasites obtained from bugs were found by Blacklock to be infective for from 21 hours to 77 days after an infective feed. There is no evidence that bedbugs play any appreciable rôle in the transmission of the disease in nature, although a related trypanosome of bats is claimed by Pringault to have been transmitted to four out of five bats by the bites of infected bat bugs, *Cimex pipistrelli.*

The situation with respect to bedbugs and relapsing fever is essentially the same, except that, in bugs which have fed on relapsing fever cases, the spirochætes may invade the body of the insect, and sometimes even the salivary glands. In a few instances relapsing fever has been transmitted to animals by bugs which had immediately before fed incompletely on infected animals, a method of transmission which is no more significant than the equally successful experiment of infecting an animal by pricking it with an injection needle which has just been inserted into an infected animal. Attempts to transmit relapsing fever experimentally by bites of bedbugs, except in this immediate mechanical manner, have invariably failed, although bugs have been shown to harbor the spirochætes for a number of weeks, and may cause infection if their crushed bodies are injected. Both the louse-borne and tick-borne strains of the spirochætes will develop in bugs without being transmitted by them. In certain cases the epidemiology suggests bedbugs, and they are constantly being suggested as possible vectors in certain localities, but in view of the numerous experiments in which definitely infected bugs have failed to function as transmitters it seems highly improbable that any strain of the spirochæte exists which differs in this respect from the others. The failure to transmit is too definitely associated with the structure or habits of the bug, and not with the viability of the parasite in this host. As in the case of leishmaniasis the possibility of an *occasional* case of infection by a freshly soiled proboscis or a crushed bug cannot be excluded, but further accusations against the bedbug as a primary factor in the dissemination of relapsing fever appear to be out of order.

In the case of infectious jaundice, caused by *Leptospira icterohæmorrhagiæ,* most attempts to transmit the infection by the bites of infected bedbugs have failed, but Blanchard and his colleagues claim to have accomplished this, between guinea pigs, by the bites of infected *Cimex lectularius,* some of which remained infective for over a month. The infection is easily transmitted by inoculating with crushed bugs.

Since the guts of bedbugs as of many other insects contain antibacterial substances, few bacteria succeed in establishing themselves in bugs. One outstanding exception is the bacillus of tularemia, *Pasteurella tularensis.* According to Francis and Lake bugs fed on infected animals retain virulent organisms in their guts for at least four months. When such bugs are eaten by mice infection results, and this is also true of inoculation of the feces even after being dried for 20 days on filter paper, yet the feces are not infective when eaten. The living bugs transmitted the disease at any time from a few seconds to 71 days after an infective feed, either by direct puncture or contamination with the feces.

Bacot has shown that plague organisms also may develop in bugs, though more slowly than in fleas and with a much higher mortality for the bugs. Experiments showed that bugs could transmit plague to mice after 48 days of starvation following an infective feed. Bugs have been suspected of playing a part in human plague transmission, but it is evident from the epidemiology that its rôle is a very minor one.

Bedbugs have frequently been suspected of harboring and transmitting leprosy germs. Sandes and Long (1911) claim to have found acid-fast bacilli in 20 of 75 bugs which had been associated with lepers, but a number of different workers have failed to confirm this, even on much larger series of cases.

The bug has also been incriminated on purely epidemiological evidence of transmitting typhoid fever in a few instances, and the suggestion has been made that the disease may frequently be spread in this manner within a building. The evidence, however, is not sufficient to warrant much excitement over this danger.

Bugs are among the many different insects which have been investigated in connection with infantile paralysis. Howard and Clark claim to have maintained the virus of this disease for seven days in bugs fed on infected monkeys. Subsequent investigators have failed to find the virus in bugs which had fed on human cases, but occasional transmissions by bugs within a family is still considered a possibility, either by direct puncture or by scratching the skin with fingernails contaminated from a crushed bug.

Frequently bugs have been " among those mentioned " as being responsible for the spread of typhus, but it is now almost universally agreed that in this case the bug is fully exonerated.

The possible relation of bedbugs to malaria is of a somewhat different nature. In Russia observations were made which showed that Anopheles mosquitoes would feed on bedbugs and lice which had recently filled up on malarial blood, and it is stated that the mosquitoes became infected in this manner. The principal practical significance of this is the possibility of malaria being spread even with careful screening of patients to prevent their being bitten by mosquitoes.

Probably bugs will be suspected of carrying many other diseases, for when other obvious transmitting agents are not discovered, it is but natural that the presence of numerous bugs should lead to speculation as to their innocence or guilt. In one epidemic of seven-day fever in the Sudan, for instance, since there was no evidence implicating other blood-sucking insects, the bedbugs, which were abundant in the barracks of the afflicted soldiers, were assumed to be responsible. Such evidence is, of course, entirely inadequate. Many epidemiologists would do well to read more detective stories, and learn that the most obvious explanation is often not the correct one.

Other Parasitic Bugs

Most of the other true bugs which may be looked upon as normally human parasites belong to the family Reduviidæ. This is a large family of rapacious bugs, many of them bright colored, which are especially numerous in the tropics. Nearly all are active runners and good fliers. They have small narrow heads, slender, filamentous antennæ, and three-jointed beaks.

No doubt the more primitive members of the family were strictly predacious on other insects and only bit vertebrates in self defence, but a number of genera have discovered that very delectable blood meals can be obtained by piercing the skins of mammals, and have more or less completely departed from the ancestral predacious habits to become blood-suckers. Some of the blood-sucking forms still voluntarily attack such insects as caterpillars and bedbugs, while most if not all of them, it seems, hark back to the ways of their forebears, especially in their earlier stages of development, by becoming cannibalistic and obtaining their blood second hand by sucking it from the bodies of their brothers and sisters.

The blood-sucking Reduviids, as Larrousse (1927) has pointed out, can be distinguished from their more conservative predacious relatives by the position of the proboscis when in repose; in the blood-suckers this organ is bent back straight or nearly so, more or less parallel with the lower line of the head, while in the predacious forms it is strongly curved. The only exception to this is in the case of the hairy *Apiomerus* which feeds on honey bees but nevertheless holds its proboscis straight; it is interesting to note, however, that a South American species referred to this genus by Larrousse is said to attack man and domestic animals. From an evolutionary standpoint it is interesting to note the difference in effects of the bites of the predacious species which only bite man in self-defense and of the truly blood-sucking forms. The predacious Reduviids, such as the kissing bugs and wheel-bugs (*Arilus*) cause intense pain by their bites; there is often a temporary feeling of faintness and nausea accompanied by other toxic symptoms, and the pain, with swelling and irritation, may persist for a week or more, and even spread from the finger to the head. In some instances almost a year is required for complete recovery. On the other hand the bites of the blood-sucking species are almost or quite painless, and ordinarily are not sufficiently irritating to awaken a sleeping person.

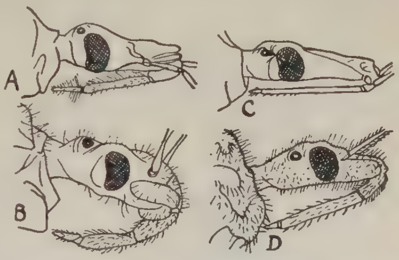

Fig. 212. Heads of various Reduviid bugs, showing point of insertion of antennæ and shape of proboscis. *A*, *Triatoma*, *B*, *Platymerus*; *C*, *Rhodnius*, and *D*, *Apiomerus*. (After Larrousse.)

The majority of the blood-sucking forms belong to the genera *Triatoma* (formerly *Conorhinus*) and *Rhodnius*. The bugs of both genera are nocturnal. In the daytime they hide like bedbugs in the cracks of walls, thatched roofs, débris on the floor, etc., issuing forth at night to feed on their sleeping hosts. They are so active and hide so rapidly when a light is produced during their foraging in the dark that they can seldom be caught.

There are numerous species of *Triatoma*, and they are found in nearly all the warm parts of the world, but are especially abundant in tropical America. Many of them are partially predacious, while others seem to be almost entirely blood-suckers. While most of them will feed on a great variety of hosts, some seem to be especially associated with certain animals. Frequently they are reported as inhabiting the burrows or nests of certain rodents, armadillos, etc. While it is probable that any of them would accept a human meal if the opportunity presented itself, the habits and habitats of the several species render some very much more frequent human biters than others. There are between 30 and 40 species of *Triatoma* described from various parts of America from

Argentina to Southern United States and California, while only a few species occur in the Old World. *Rhodnius* contains six species, according to Larrousse (1927), all found between Brazil north of the Amazon and Central America. The species of this genus are readily distinguished from those of *Triatoma* by the position of the antennæ, which in *Rhodnius* are situated near the apex of the head while in *Triatoma* they are at some distance from it. (See Fig. 212.)

The most important species of *Triatoma* is the "barbeiro," *T. megista* (Fig. 213), since it is the normal transmitter of *Trypanosoma cruzi* in Brazil. This is a large, handsome black insect trimmed with red, which is widely distributed in Brazil and occurs also in Peru and British Guiana. It is thoroughly domestic in its habits, and normally lives in the huts of the natives, feeding on the inhabitants at night although no doubt it also feeds on other animals in or around the houses. The life cycle of this as of other members of the genus is similar in general to that of the bedbug. The eggs are white, oval objects when first laid, soon turning yellowish and then brownish; they are laid in small batches in crevices in the walls of the houses; the total number laid by a female is from 200 to 300. The eggs require several weeks to hatch, the time depending largely on temperature. The young wingless insects which emerge, usually called "larvæ," are at first light in color and subsequently darken; they take their first feed several days after hatching, and feed a second time at the end of about fifteen days. The first moult takes place at the end of about six weeks, and the so-called first nymphal stage is entered upon, the insect then having short rudimentary wings. There are in all five moults before the mature adult stage is reached, the whole life cycle requiring approximately a year.

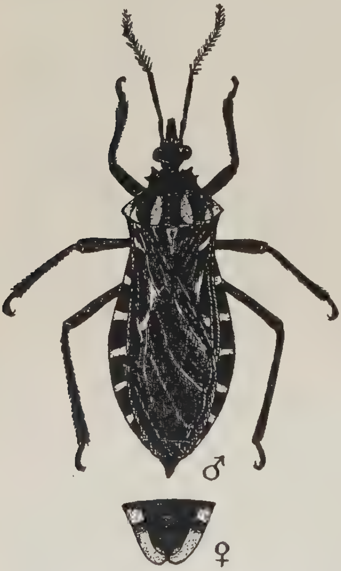

Fig. 213. The "barbeiro," *Triatoma megista*. × 1½. (After Chagas.)

From Southern Brazil to Argentina and west to Bolivia and Chile *T. megista* is replaced by another house-infesting species, *T. infestans*, known in Argentina as the "vinchuca." This is the species whose habits were vividly described by Darwin in his "Voyage of a Naturalist." Like *T. megista* it is a bold and vicious biter, but its bites are almost painless. It is not as thoroughly domestic in its habits as is *T. megista.*

Most of the other species of *Triatoma* pay their attentions primarily to rodents, armadillos or other wild animals, but many of them frequently enter human habitations to bite if not to breed. Both *T. protracta* of California, Arizona and Mexico and *T. sanguisuga* of the Gulf states are of this semi-domestic type; they are frequently known as "big bedbugs," "Mexican bedbugs," etc., since in the nymphal stages, in which the wings are still rudimentary, they superficially resemble bedbugs except in the shape of the head and thorax. The wide-spread *T. rubrofasciata* of the Old World, found from southeastern Asia to Africa and Madagascar, and represented by a closely related if not identical species (*T. mexicana*) in tropical America, is also a semi-domestic form which apparently enters human habitations only to bite; it is thought by Patton and Cragg that it probably inhabits the nests of some arboreal mammal. It is of interest as having been under suspicion as a carrier of kala-azar, and also because it harbors a trypanosome which has been suggested as possibly pathogenic to man (see below).

Of the species of the genus *Rhodnius, R. prolixus* ranks with *Triatoma megista* in importance, for not only is it primarily a human parasite, but in northern South America it replaces *T. megista* as the transmitter of *Trypanosoma cruzi.* This bug is brown with yellowish markings, much lighter in general color than most of the species of *Triatoma.* Although the insect is said by some writers to inhabit the burrows of armadillos and also of a common Venezuelan rodent, the brown Paca (*Cœlogenys subniger*), Uribe (1927) failed to find it except in human habitations. Its life cycle is similar to that of *Triatoma,* except that there is only one feeding in each of the first four stages, whereas in the final nymphal stage it feeds a number of times. The entire life cycle occupies from five months to a year, probably largely dependent on temperature and frequency of feeding. The adults and even the young nymphs can live for a number of months without food. Uribe made the interesting observation that at a temperature of 98.6° F. the eggs fail to hatch even when provided with plenty of moisture. The other species of *Rhodnius* seem to be less strictly human parasites, but at least one of these, *R. brumpti,* has been shown to be an intermediate host of *Trypanosoma cruzi.*

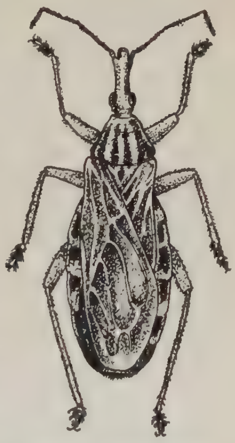

FIG. 214. *Rhodnius prolixus.* × $2\frac{1}{4}$. (After Larousse.)

Other reduviid bugs which are not normally blood-suckers often bite man when interfered with, and their bites, as remarked above, are far more painful and toxic than those of the true blood-suckers. One species, *Acanthaspis sulcipes*, has been thought to be the possible transmitter of a form of endemic goiter in tropical Africa. In North and Central America there are a number of species of "kissing bugs" and "corsairs" of the genera *Melanolestes*, *Reduvius* and *Rasahus*. The common kissing bug or "black corsair," *Melanolestes picipes*, became very abundant in the United States a few years ago and gave opportunity for many startling newspaper stories. The wheel bug, *Arilus cristatus*, is another very vicious biter. Hall (1924) reports one case in which its toxic effect caused papilloma-like growths on a finger which lasted for several months, and there was a feeling of warmth in the finger for a year. There are also many Hemiptera of other families which produce similar painful bites, and they are all best not handled with the bare hands. One which is worthy of special mention is the malodorous pito bug, *Dysodius lunatus* (Fig. 215) of South America, belonging to the family Aradidæ. It is a large broad bug which frequents houses and bites severely.

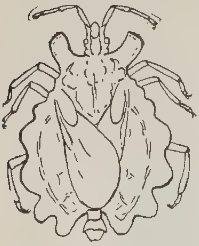

FIG. 215. Pito bug, *Dysodius lunatus*. (After Alcock.)

Blood-sucking Reduviids and Disease. — A considerable number of the species of *Triatoma* and two of *Rhodnius* in South and Central America have been found to be capable of acting as intermediate hosts of *Trypanosoma cruzi* or a species which is morphologically indistinguishable from it. *Triatoma megista*, *T. infestans* and *Rhodnius prolixus* are the most important natural transmitters of the disease, since these three species, more than any others, live and breed in human habitations and habitually feed on human blood. Another species, *T. sordida*, also frequently invades houses, but is commoner in the vicinity of running streams. It is said, however that this species is the only one present in some localities where Chagas' disease occurs. (See p. 154.)

Triatoma megista seems to be the species most frequently involved in human transmission in the greater part of Brazil. It abounds in the mud-walled, palm-thatched houses, often accompanied by *T. sordida*, but naturally infected *megista* are much commoner than *sordida*. *T. infestans* is very frequently infected not only in the southern part of Brazil, overlapping the range of *T. megista* in São Paulo, but also in Uruguay, Paraguay, and Argentina. A high percentage of infected bugs are found in some parts of Northern Argentina where Chagas' disease, if it occurs at all, is rare, and in the cases of goiter which do occur in the mountainous districts of some of the northern provinces no trypanosomes have been demonstrated in the blood.

In Venezuela and Colombia the stellar rôle in the transmission of human trypanosomiasis is taken by *Rhodnius prolixus*, which has habits very similar to those of *T. megista*.

There are certain habits of blood-sucking Reduviids which are of interest in connection with the transmission of trypanosomes. Cannibalism is a common habit among many if not all of the species of *Triatoma* and *Rhodnius*. The habits, especially of young larvæ, of sucking blood from the distended bodies of their brothers and sisters or of older individuals, usually of their own species, is a common one. Strangely enough the bugs which are robbed of their meals seem to be quite untroubled and unharmed by it. Perhaps like the Romans of old they are glad to get rid of their meals in order to be able to enjoy the ingestion of more. That infection is spread from bug to bug in this manner is a well-established fact.

Rhodnius has another habit which serves to spread infection from bug to bug, namely the ingestion of liquid feces of other bugs. This coprophagous habit seems not to be shared by the species of *Triatoma.*

Hereditary transmission of trypanosomes apparently does not occur. The percentage of infected individuals steadily increases with age up to the adult stage. This, in part at least, accounts for the seasonal incidence of acute cases of Chagas' disease in the hot months, since the adults and older nymphs are commonest in the hot season.

Except for the transmission of *cruzi*-like trypanosomes, Reduviids have not been definitely incriminated as disease carriers. Other species of trypanosomes, such as *T. equinum* and *T. gambiense*, disappear from the guts of *Triatoma* soon after the infected blood has been ingested. Suggestions as to the possible transmission of kala-azar by *Triatoma rubrofasciata* have been made but there is no evidence of the truth of this hypothesis. The crithidial and herpetomonad forms described in some species of *Triatoma*, *e.g. Crithidia conorhinæ* in *T. rubrofasciata* in India, may be interpreted as purely insect flagellates or as possible intermediate stages of vertebrate trypanosomes, or, still better, as parasites which might be able to exist as trypanosomes in vertebrates on which the bugs habitually feed. That the latter is true has been demonstrated by Shortt, who inoculated mice with *Crithidia conorhinæ* and obtained trypanosomes in the blood.

Remedies and Prevention

Prevention of "bugginess," at least in the case of bedbugs, consists chiefly in good housekeeping, but occasional temporary infestations are likely to occur in almost any inhabited building. A number of remedies for bugs have been advocated, of which the best is undoubtedly fumigation with hydrocyanic acid gas, as described below. Sulphur is also valuable for fumigation but is not so harmless to household goods as is hydrocyanic acid gas. When the infested parts of houses or rooms can be located easily, good remedies are kerosene, gasolene, turpentine, toluene or other coal-tar products painted or injected with a squirt gun into all the infested cracks and crevices, especially in the woodwork of beds. An effective remedy of this nature is a mixture of one ounce corrosive sublimate, two cups alcohol, one-half cup turpentine. These substances should be applied several times at intervals of a week in order to destroy newly hatched bugs. Some housekeepers take infested beds apart and pour boiling water into the " buggy " parts, thus effectually killing both bugs and eggs in the bed, but this does nothing against bugs which may hide elsewhere than in the bed. Bedbugs have a number of natural enemies, among which may be mentioned especially cockroaches, red ants and large predacious bugs, but all of these are pests themselves, and are, therefore, hardly to be encouraged as bedbug hunters, efficient as they might be in this capacity.

Although bedbugs are very resistant to cold, they succumb to rather moderate heat. Newly-hatched bugs are killed by a few days of humid heat at 98° to 100° F., and with temperatures of 110° to 120° they are killed in a few hours. Steam-heated rooms can easily be rid of bugs by applying the heat on a summer day, and maintaining a fairly high temperature for a few hours. The higher the temperature the more quickly it will penetrate into mattresses, upholstered furniture, etc.; usually a room can be completely disinfested by a temperatue of 120° in six or eight hours. Even in bunk-houses which are not equipped with steam heat, pipes can often be run in with little labor, and vermin destroyed more easily than by fumigation methods.

Fumigation

Hydrocyanic Acid Gas. — Of the remedies for bugs mentioned above, fumigation with hydrocyanic acid gas is the most effective. This gas can be used with good success for fumigation of houses, mills, granaries, greenhouses or any other closed structure, against any kind of insect pest. But since the gas is extremely poisonous not only to insects but also to other animals and to man, its use must be accompanied by great care and precaution. A few deep breaths of the gas is sufficient to cause asphyxiation. On the other hand it has great advantages in that it is not inflammable or explosive, and, unlike sulphuric fumes, does no damage to dry foods or to household goods, except to tarnish nickel slightly. Wet foods may absorb some of the gas and should be removed before fumigation. Care should also be taken that there is no possible avenue of escape for the gas into adjoining rooms or houses which are occupied. The characteristic peach-kernel odor, however, makes its detection easy, thus removing danger of asphyxiation without warning.

One method of generation of the gas is by the action of sulphuric acid on potassium or sodium cyanide. The procedure as advised by Herrick is as follows: Estimate the number of cubic feet in the room or house to be fumigated, and allow one ounce of potassium cyanide to every 100 cubic feet. Make the room or house as near air tight as possible, stopping all the large openings such as fireplaces and chimney flues with old rags or blankets. Seal cracks about windows and doors with strips of wet newspaper. Such strips when thoroughly wet can be applied quickly and effectively over cracks and will stick tightly for several hours, and can be removed easily after the operation. While the room is being made tight someone should measure out the required ingredients for fumigation, allowing one fluid ounce of crude sulphuric acid and three fluid ounces of water to each ounce of potassium cyanide. The water first should be poured into a stone crock holding two gallons or more, *i.e.*, large enough so that the reacting fluid will not spatter on floors or carpets. The crock had best be placed on several thicknesses of newspaper or on an old rug or burlap sack. The required amount of sulphuric acid should then be poured slowly into the water. *Never* pour the water into the acid. The cyanide should be weighed out and put into a paper bag beside the jar. All articles which might suffer from the gas or which will be needed before the operation is over should be removed from the room. When everything is ready the operator, holding his breath, should drop the paper bag of cyanide gently into the acid jar, and walk out shutting the door behind him. The time required for the acid to eat through the paper bag in order to reach the cyanide gives ample time to leave the room before the steamlike gas arises. If preferred, however, the paper bag may be suspended by a string passing through a screw eye in the ceiling and through the key hole of the door (Fig. 216). The operator may then lower the bag into the jar after leaving the room.

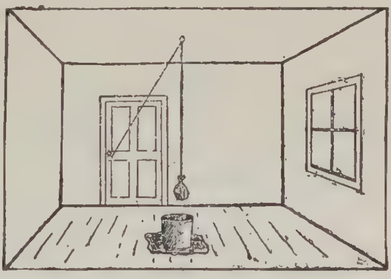

Fig. 216. A room "strung" for hydrocyanic acid gas fumigation from outside. The bag of cyanide can be lowered into the crock of sulphuric acid and water by means of the string. (After Herrick.)

When stringing a room in this manner, care should be taken not to place the acid jar under the bag until everything is ready. The fumigation should extend over a period of five or six hours at least, a good method being to start the operation toward evening and let it run all night. Better results will be obtained at a temperature of 70° F. or above, than at a lower temperature.

Two or three hours after the doors and windows have been opened the gas will have disappeared sufficiently to allow safe entrance into the room, though it should not be occupied until the characteristic odor is gone. The contents of the generating jar should be dumped in some safe place and the jar washed before being used again. When a whole house is to be fumigated each room should be made ready as described above and then set off in regular order beginning on the upper floor and working downward, since the gas is lighter than air and therefore rises. Herrick describes clearly and in detail the method which he has successfully used in the fumigation of large dormitories. For this account the reader is referred to Herrick's "Insects Injurious to the Household."

The effectiveness of this method of fumigation against bedbugs was proven by experiments conducted by Herrick. Bugs were placed in perforated pill boxes and wrapped in various manners, some with three inches of excelsior, some in two folds of a thick comforter, some in two inches of cotton batting and others in two folds of a woolen blanket. Others were placed in a cork-stoppered vial, the cork of which was punched twice with a pair of curved forceps. In each box several newly laid eggs were enclosed to determine the effect of the gas on their hatching. In every case every bedbug was killed and none of the eggs showed signs of hatching in 12 days. According to experiments made by the U. S. Public Health Service five ounces of powdered potassium cyanide per 1000 cubic feet is sufficient for the destruction of bedbugs, four ounces for mosquitoes, two and one-half ounces for fleas and ten ounces for lice.

Recently calcium cyanide has been substituted for the use of sodium cyanide, since no acid is necessary and much time and some expense can be saved in the fumigating process. The calcium cyanide is obtainable in tight containers in the form of dry granules or powders containing between 40% and 50% of the chemically pure substance. When acted upon by the moisture of the air the cyanide, $Ca\ (CN)_2$, is converted into lime and hydrocyanic acid gas. It is only in moist air that this method of fumigation is effective.

After the openings of a room have been sealed up and everything is ready for fumigation the calcium cyanide is spread in a thin layer, about $\frac{1}{8}$-inch thick, on newspapers on the floor; about two pounds is used for each 1000 cubic feet of space. At the beginning of fumigation the concentration of the poison gas in the air is low, so that there is little danger to the fumigator in starting the process, and he has ample time to leave the room or building. It has been experimentally shown that a minimum concentration of 0.3% of hydrocyanic acid for three hours kills all bedbugs, fleas, lice and other insects, and their eggs, if it reaches them, and that in closed spaces the quantity of calcium cyanide designated above gives this concentration in about 1½ hours, and maintains it for a number of hours, according to the thoroughness of the closing up of the room. Unless this concentration is maintained for a few hours the fumigation is ineffective. It is probable that in rooms which cannot be very tightly sealed a higher concentration could be maintained by using a larger quantity of calcium cyanide, since it is only necessary that after the effective concentration is reached the gas be evolved as rapidly as it is dissipated.

Sulphur. — The fumes of burning sulphur, sulphur dioxide, rank next to hydrocyanic acid gas as both a disinfectant and an insecticide, but they have a serious disadvantage in their tendency to bleach fabrics and to tarnish metals, especially in a humid atmosphere. Sulphur dioxide is considered the most effective remedy for mosquitoes in cellars, barns, etc., since it kills these insects even when very dilute, and it has remarkable penetrating power. The methods of sealing rooms or buildings are similar to those described for hydrocyanic acid fumigation. All dyed goods and metallic articles, however, must be removed or covered with vaseline. Three pounds of sulphur is used to 1000 cu. ft., more if the building cannot be tightly sealed. The sulphur is placed in a conical pile in some suitable dish with a little wood alcohol poured in a depression at the top to make it burn more readily. In order to avoid danger of fire, the dish of sulphur should be placed on bricks or in a tub of shallow water before igniting. After two hours the place may be opened and ventilated.

Other Fumigants. — Another effective insecticide is the vapor of carbon bisulphide, a poisonous gas which is not nearly so virulent as hydrocyanic acid gas. As its vapor is heavy it settles rapidly. Its effect on many insects is less certain than in the case of the hydrocyanic acid gas and it has the additional disadvantage of being both inflammable and explosive. Recently cresyl or creolin, a very volatile substance, has come into favor as a fumigating medium, especially for destroying mosquitoes. It is not injurious to higher animals in the strength used (125 cc. to 1000 cubic feet), does not injure household goods and is destructive to all exposed insects. It is volatilized by means of an alcohol lamp. Cresyl does not. however, have the penetrating power of hydrocyanic acid gas or sulphur, and is therefore of less value for such secretive insects as bedbugs, though highly valuable for exposed insects, such as mosquitoes, since they may be destroyed without having the rooms vacated. Formalin, well known as an active disinfectant, is not usually considered an effective insecticide. Some experiments have been made, however, which showed that when formalin is vaporized by dropping into it chloride of lime at the rate of two pounds to two pints of formalin for each 1000 cu. ft. of space, bedbugs are killed under favorable conditions, namely a temperature of 70° or over, high humidity, and generation of the formalin vapor at a high level in the room, since it is heavier than air. None of these fumigants, however, have the penetrating power of hydrocyanic acid.

CHAPTER XXIV

LICE

Although the disrepute of human lice has grown with civilization and with the knowledge that lousiness and cleanliness are incompatible, lice are even yet among the most important of external human parasites. In former times the louse apparently was not an object of disgust and loathing even among the better class of people. In Herrick's entertaining book, "Household Insects," the following quotation from Hooke, an English zoölogist of the 17th century, is given concerning the head louse. "This is a creature so officious that 'twill be known to everyone at one time or another, so busie, so impudent, that it will be intruding itself into everyone's company, and so proud and aspiring withall that it fears not to trample on the best, and affects nothing so much as a crown; feeds and lives very high, and that makes it so saucy as to pull anyone by the ears that comes its way, and will never be quiet till it has drawn blood."

Unfortunately, even at the present time, and in the face of present knowledge concerning the rôle of lice in the spread of disease, there are many individuals, many communities and even some races which make no effort to exterminate them. Still more unfortunate is it that there are many people who of necessity must associate with these unwelcome companions. In logging camps, jails, ships, railroad camps, etc., where close association with people who are dirty by nature is unavoidable, lice very often become prevalent. Most of all, however, are lice associated with war. The deadly typhus fever, which has ravaged the armies of almost every war in the history of the world, as far as is known, apparently is spread exclusively by lice. These parasites are the guerillas of war; they bring suffering and death not only to armies but also to the innocent non-combatant population of the war-stricken countries through which the armies have passed. This phase of the subject will be discussed in more detail under the section on "Lice and Disease."

General Structure. — Lice are small wingless insects of which there are two quite distinct groups: the sucking lice, constituting the order Anoplura, and the biting or bird lice, constituting the order Mallophaga. The former are all mammalian parasites, while the latter are for the most part parasites of birds, though there are a number of them which choose to infest mammals. The Mallophaga have nipper-like mandibles fitted for chewing instead of sucking, and they feed only on hair, feathers and epidermal débris, and not at all on blood, whereas the Anoplura have piercing mouthparts and nourish themselves on the blood of their hosts. In other respects these two groups of lice show many structural resemblances to each other and are now generally believed to be more or less distantly related, but it is impossible to determine how much the resemblances may be due to convergent evolution as a result of a parasitic form of life, and how much to actual relationship. Since the Mallophaga do not pierce the skins of their hosts they can have no part in the transmission of disease; they are nevertheless often injurious to their hosts as a result of irritation of the skin surface, and may be the cause of much unthriftiness by the annoyance and insomnia which their activities cause. The Anoplura, on the other hand, like all other blood-suckers, are potential and in this case actual disease transmitters. The lice of these two orders are readily distinguishable by the presence in the Mallophaga, and absence in the Anoplura, of the heavily chitinized mandibles which are brown or blackish in color, but they can also be distinguished at once by the fact that the Mallophaga have very broad heads, always broader than the thorax, whereas the Anoplura have the head always narrower than the thorax. Since none of the Mallophaga are human parasites, we will not be concerned further with them.

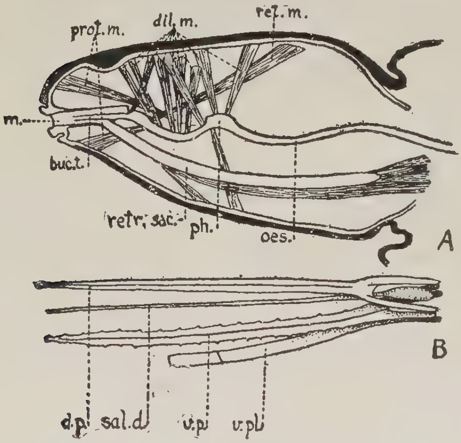

Fig. 217. Mouthparts of a body louse; *A*, longitudinal section through head; *B*, mouthparts from sac under pharynx and esophagus; *buc. t.*, buccal tube; *m.*, mouth cavity; *ph.*, pharynx; *oes.*, esophagus; *retr. sac.*, retractile sack for mouthparts; *prot. m.*, protractor muscles of pharynx; *ret. m.*, retractor; *dil. m.*, dilators; *d. p.*, dorsal piercer; *sal. d.*, salivary duct; *v. p.*, ventral piercer; *v. pl.*, ventral plate (= labium ?). (Adapted from Harrison.)

The Anoplura have the body clearly divided into a narrow and often elongate head, a broad thorax, and an abdomen which is more or less distinctly divided into segments. The sexes are distinguishable by the fact that the terminal segment of the abdomen is indented in the females, while in the males it is rounded, with the large spike-like copulatory organ often projecting at its tip. The body is provided with numerous spines and bristles, and there is a row of spiracles along the sides of the abdomen, a pair on each segment, by means of which the insects breathe.

The head is provided with short antennæ and, in some species, a pair of prominent but not compound eyes. The legs, except in one genus found on elephants, are armed each with a very large curved claw, quite grotesque in appearance in some species, which closes back like a finger against a thumb-like projection of the next segment, the tibia, of the leg (Fig. 219). There are not even rudiments of wings.

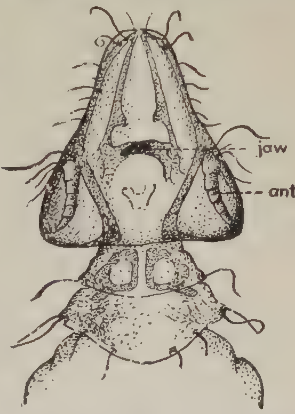

Fig. 218. Head of bird louse (from golden eagle); *ant.*, antenna. Note breadth of head as compared with thorax, a feature which readily distinguishes bird lice from sucking lice.

The piercing mouthparts, when not in use, are retracted into a little pouch under the pharynx (Fig. 217). There is a chitinized ventral plate which possibly represents a labium. There are two piercers, dorsal and ventral, forked at their posterior ends where they are attached, and each showing evidence of being originally double; imbedded in the ventral one is a delicate salivary duct through which the salivary fluid, which has the power of preventing blood from coagulating, is injected. The blood is sucked through a canal formed by the dorsal piercer.

The stomach is provided with lateral pouches in order to increase the food capacity. Rapid digestion and absorption takes place in the stomach, both red and white blood corpuscles being completely digested in a few hours. Normally lice do not fill themselves to repletion and then wait until this is digested before feeding again, but instead they enjoy more moderate meals at frequent intervals.

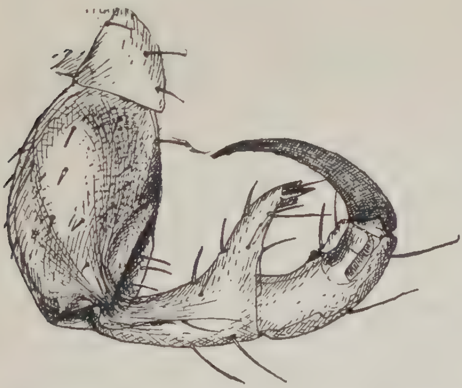

Fig. 219. Front leg of body louse, *Pediculus humanus*. Note huge claw and thumb-like opposing process of next segment. × 100.

Most species of lice are quite closely limited to a single host, and sometimes even genera are thus limited. Kellogg has suggested that the evolutionary affinities of different birds and mammals may be demonstrated by the different kinds of lice which infest them.

The lice which infest man and other Primates all belong to the family Pediculidæ, which are distinguished from the related Hæmatopinidæ of other mammals by the presence of eyes. The lice infesting man belong to two genera, namely *Pediculus*, including the head and body lice, and *Phthirus* with only a single species, the human crab louse. Other species of *Pediculus* occur only on the anthropoid apes and in the South American spider monkeys of the genus *Ateles*. The *Ateles* lice have been placed in a separate subgenus by Ewing; it is an interesting question whether these lice spread from man to spider monkeys, which approach man in the texture of the hair and also in the nature of the blood, or developed independently from the human lice from some remote ancestors which infested the fore-runners of both *Ateles* and the higher apes and man. The former hypothesis appears more probable.

Head and Body Lice. — For a long time these two kinds of lice were regarded as quite distinct species, but the more recent tendency is to regard them as mere varieties of one species, *Pediculus humanus*. The head louse, formerly known as *P. capitis*, becomes *Pediculus humanus humanus*, while the body louse, formerly known as *P. corporis* or *P. vestimenti*, becomes *Pediculus humanus corporis*. No doubt both of these lice are the descendents of a species which roamed the hairy bodies of our forefathers in the pre-caveman days. With the developing hairlessness of its host the hunting grounds of the lice became more and more restricted, and they withdrew to the fine hair of the head where they found conditions more suitable than in the residual coarse hair of other parts of the body. With the differentiation of the principal races of man some slight differentiation of the lice also occurred; Ewing recognizes four varieties found on Caucasians, Negroes, Chinese and American Indians, respectively. It is difficult, nowadays, to find these races of lice pure; they interbreed, and the intermixture of lice between different human races has resulted in as much hybridization as has occurred in the human race itself. Studies of ethnology of lice and of man are beset with similar and largely identical difficulties.

The body louse, less conservative than the head louse from which it probably sprung, inhabits the clothing instead of the hair of its host; the German name " Kleiderlaus " is a much more accurate name. It is possible that this louse developed independently from the ancestral " ape-man louse " shifting its position from the waning hair to the more and more habitually worn clothes, but it is more likely that it developed from the head louse; it is a true radical in its habits, since of all the lice in the world it alone lives elsewhere than in the hair of its host. A person infested with thousands of body lice may remove his clothing and find not a single specimen on his body. An examination of the underwear will reveal them adhering by their long claws to the surfaces which were next to the body. Here they live and lay their eggs, merely reaching across to the body to suck blood, usually retaining a hold on the clothes by their hind legs. Whether or not body lice have developed from more than one of the races of head lice, or from which one it developed, is not known. Bacot has observed that body lice and head lice will interbreed, and Nuttall has shown that all of the supposed morphological and biological differences between these two kinds of lice are inconstant. As a rule body lice are somewhat larger than head lice, and have the abdomen less distinctly festooned along the sides by the constrictions between the segments. When the head louse is reared under conditions suitable for the body louse it assumes the characteristics of the latter.

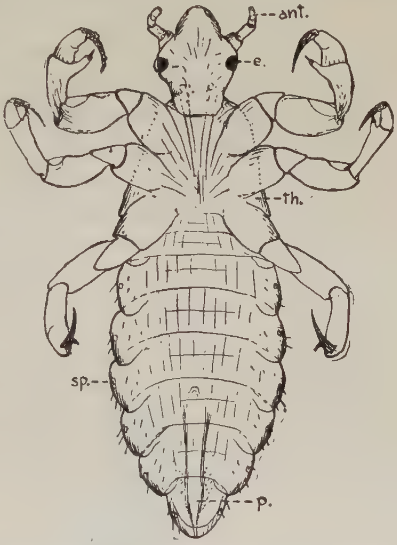

FIG. 220. Body louse, *Pediculus humanus*, male; *ant.*, antenna; *e.*, eye; *p.*, penis; *sp.*, spiracles; *th.*, thorax. × 25.

The general appearance of head and body lice can be seen from Fig. 220. The females, which are somewhat larger than the males, reach a length of about 2.5 to 3.5 mm., averaging somewhat larger in body lice than in head lice. Due to the common dirty white or grayish color, body lice are sometimes called "gray-backs," but since the war, when lice enlarged their acquaintanceship so extensively, the more familiar name "cootie" has come into general use. Lice change color to match their environment, and may vary from almost white to brown, reddish, gray or nearly black, the change occurring in a couple of days. It is obvious, therefore, that color cannot be used for differentiating varieties, even though they do somewhat resemble in color the skin of the human races on which they live. What a wonderful case of protective coloration, except that, as in so many other cases of so-called protective coloration, there is no practical protection. A negro is as likely to scratch out a black louse as a white one!

The preferred habitat of the head louse is the fine hair of the head, though it occasionally wanders to other parts of the body. It occurs on all races of man and in every part of the world. The body louse, on the other hand, lives on the clothing next to the skin; a few of them are frequently found attached to the hair of the arm pits, chest or pubis, but they are probably there only temporarily while obtaining a meal. Body lice do not exist among those races of man who wear only beads and perhaps a loin cloth.

Habits and Life History. — Although there has been very close association between lice and human beings probably since man's first appearance in the world, little definite knowledge concerning the life history of any of the three species was obtained until recently. The importance of lice in the great war stimulated much research on them.

One of the first experiments with the breeding of body lice was made by the great zoölogical pioneer, Leeuwenhoek, in the 17th century. He placed two female lice in his stocking and tied them in; after six days he opened the brood chamber and found a cluster of 50 eggs beside one of the lice and another cluster of 40 eggs, probably laid by the other insect which had escaped. He found 50 more eggs in the remaining louse. He left the eggs in his stocking ten days more, when he discovered 25 young lice, whereupon he abandoned his experiment in disgust.

The eggs of lice, commonly called "nits," are oval, whitish objects fitted with a little lid at the larger end, through which the hatching takes place. The eggs of head lice are slightly less than one mm. in length, and are glued by the lower end, by means of a cement-like excretion, to the hairs (Fig. 221*A*), the favorite "nests" being the vicinity of the ears. The average number laid by each female, according to Bacot, is from 80 to 100. Body lice lay slightly larger eggs and glue them to the fibers of the clothing, especially along the seams or creases. Under experimental conditions the body louse will sometimes lay eggs on hairs, but it nearly always selects the crossing point of two hairs and shows less skill than the head louse in attaching the eggs. The body louse shows a marked "homing" instinct in laying her eggs, and tends to cluster them until 50 or 75 have been collected. According to the observations of Bacot in England and Sikora in Germany the total number laid may reach 200 or more; in one case 295 eggs were obtained from one female. During the first three or four days only two to four

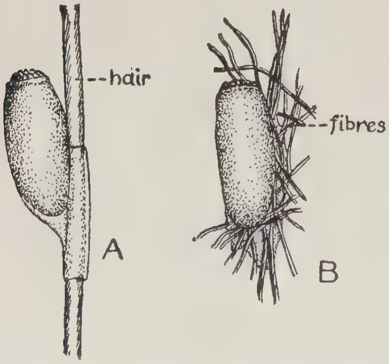

Fig. 221. *A*, egg of head louse; *B*, egg of body louse. × 25. (After Cholodkowsky.)

eggs are laid daily, the number gradually rising, until after a week or so of egg-laying seven to ten or more eggs may be laid each day although there is never more than one developed egg in the body at a time. A day or two before the end of egg-laying and the death of the louse the daily number drops again. Eggs are laid whether copulation has occurred or not, but in no case have unfertilized eggs been observed to develop. One copulation is not sufficient to fertilize all the eggs, but fertile eggs may be laid for at least 20 days after a single copulation. According to Sikora, copulation normally takes place at intervals of from one to three days. Egg-laying ceases at temperatures below 77° F. and a daily exposure to a temperature of 60° F. for only two or three hours causes a marked falling off in egg production.

According to Sikora the eggs hatch in about 6 days at a temperature of 95° F. The optimum temperatures, at which the highest percentage of hatching occurs, is around 80°, the incubation period being then about 8 to 10 days. At a temperature of 77° F. the incubation period is prolonged to 16 days, whereas at 68°, lowered to from 42° to 60° F. during the latter part of the night, or at a constant temperature of 60° F., no hatching at all takes place. At temperatures above 95°, also, the eggs suffer a high mortality probably due to the difficulty in obtaining proper conditions of humidity rather than to the direct effect of the heat itself. Either excessive humidity or complete drying is fatal to the eggs. It is evident that in winter the laying off of the clothing at night in a cold room or the leaving of mattresses or bed clothes in the daytime is sufficient to prevent the laying of eggs or the hatching of eggs already laid, thus resulting in a great reduction in numbers. The young lice have an interesting way of escaping from the eggs, by sucking air into the body and expelling it from the anus until a cushion of compressed air is formed sufficient to pop open the lid of the egg.

The newly hatched lice are almost perfect miniatures of the adults, and are ready to feed almost as soon as they emerge from the egg; in fact, they usually die in less than 24 hours if not allowed to feed, though the adults can survive as much as five days of starving. According to Sikora, the rapidity of the development of lice is dependent on temperature and on amount of food. At a temperature of 95° F. and with as many daily feeds as would willingly be taken, namely six, the lice pass through the first moult in three days, the second in five or six days, and the third, which brings them to maturity, in eight or nine days. Reduction of daily feeds to two increased the period of development to nine or ten days, whereas reduction of temperature to 75° F. by day and 65° F. by night, with two daily feeds, prolonged the development to from 13 to 15 days.

According to observations by Sikora, copulation may take place within ten hours after the last moult has been passed, and Bacot also observed cases in which copulation took place on the day of reaching maturity. Egg-laying begins in from one to four days after the final moult and continues at the rate described on the preceding page until the death of the insect. The average length of life for the females is about 35 or 40 days, and probably a little less for the males.

According to Bacot, hungry lice do not show a tendency to wander on the skin, but proceed to pierce the skin and suck blood at once. Nor do they shift to make another stab, as fleas frequently do, if the first stab does not immediately furnish blood. They apparently place great reliance on the power of the salivary secretion, which is poured into the wound, to dilate the capillaries by its irritation and thus cause a flow of blood. Sometimes blood is not drawn for several minutes after the puncture is made. Bacot states that lice fill their crops in from two to 15 minutes, but Sikora observed that adult lice, if fed only twice daily, sucked for an hour to an hour and a half, and, if left in contact with the skin for several hours, have a tendency to pump blood intermittently with short pauses, meanwhile voiding excrement containing undigested blood corpuscles. Sikora also observed that hungry lice placed on the well-shaved skin of a puppy made repeated attempts to draw blood without success, and also that dog lice, *Hæmatopinus ventricosus*, tried in vain to draw blood from the human skin. She concludes therefrom that not only is it necessary for lice to penetrate the skin with their piercing apparatus, but that they must also produce an irritation by means of a salivary secretion, apparently specific in its action for certain kinds of blood, in order to cause blood to flow from the tiny puncture. Apparently the salivary secretion deteriorates in unfed lice, for though starved lice may still be able to drive their piercing apparatus into the skin, it takes them three times as long to draw blood.

At high temperatures lice can withstand starvation for only 2 or 3 days, but at 42° F. they can live for 9 or 10 days without food. The adult lice stand exposure to cold very well, but they are destroyed by humid heat above body temperature, and die in 10 to 15 minutes in hot air at 122° to 126° F.

A fact of far-reaching significance, if found to be commonly true, has been reported by Hall in Texas. This author found that a female body louse taken from a Mexican baby, when placed in a bottle with a head louse taken from the same baby, devoured the head louse. Two head lice were then fed to the body louse daily for three days, and the same louse was induced to eat crab lice, small black ants, bedbugs, and raw beef. When body lice were placed in a bottle with head lice, bedbugs, and a piece of beef, they ate first the head lice, then the bedbugs, then the beef, and finally became cannibals to the extent of the survival of the fittest! This would readily explain such facts as that body lice (according to Hall) can be found in empty box cars used to transport Mexican troops weeks before, and it would account for louse-borne diseases lying dormant in isolated places. A freight car once infected with typhus would be a source of danger for a longer period than the few days a louse can live without food. However, before insectivorousness can be admitted as a usual habit of lice in the absence of normal food, further investigation is necessary.

Digestion is very rapid. An entire meal may be digested in from eight to ten hours at 95° F., but digestion is slower at lower temperatures and the stomach contents remain unchanged for ten hours or more at 45° F. or below. At temperatures above 95° F. digestion is even more rapid, but there is a high mortality.

It is evident from Sikora's experiments that 95° F. is the maximum favorable temperature for the development and reproduction of lice. The absence of lice from hot countries — observable in Mexico, for instance, where they are abundant on the central plateau above 5000 to 6000 feet, but absent from the hot coastal strips — is apparently not due to the high temperature but probably to the disastrous effect of profuse perspiration and consequent excessive humidity between the clothes and skin. Head lice are found in hotter countries than body lice, especially in bare-headed people.

The bites of lice produce very little local irritation, and do not regularly cause the wheals which form at the site of the bites of many insects. A sufficient amount of itching is produced to cause scratching, and the scratched bites, oozing blood or serum and often becoming infected, frequently develop into pustules and become covered by brownish scabs. Often scratching produces characteristic white scars surrounded by brownish pigment, and large areas of the skin may take on a mottled bronze color. The coloring of the skin is said to be due to stimulation of pigment formation by the toxic salivary juice. In negligent individuals the scratched bites of head lice may cause the hair to become matted. According to Stiles, if this is allowed to continue, a regular carapace may form, called trichoma, in which fungus growths may develop and under which the lice abound, and the head may exude a fetid odor. Although the direct local irritation of louse bites is mild, and many individuals develop an insensibility to them which makes some people, as in parts of Russia and Poland, very indifferent to them, the effect of the bites has been shown by Moore (1918) to be sufficiently toxic, when a person is bitten daily by large numbers of the insects, to cause a general skin eruption, mild fever, and a very marked feeling of tiredness and irritability.

Crab Louse. — The crab louse, *Phthirus pubis* (Fig. 222), is quite distinct from the other two species of human lice. It has a very broad short body with long, clawed legs, presenting the general appearance of a tiny crab, from which it derives its name. The first pair of legs are smaller than the others and do not possess a "thumb" in apposition to the curved claw. The abdomen is composed of six segments, and is markedly festooned along the sides. This louse is grayish white in color, with dark shoulder patches and slightly reddish legs. The females are about 1.5 to 2 mm. in length, the males somewhat smaller. The favorite haunts are the pubic regions and other parts of the body where coarse hair grows, as in the armpits and in the beard, eyebrows and eye lashes. Occasionally they infest almost the entire body except the head; the writer once saw a hairy individual who was covered with them from chest to ankles. Unlike the other human lice this species is almost exclusively confined to the Caucasian race.

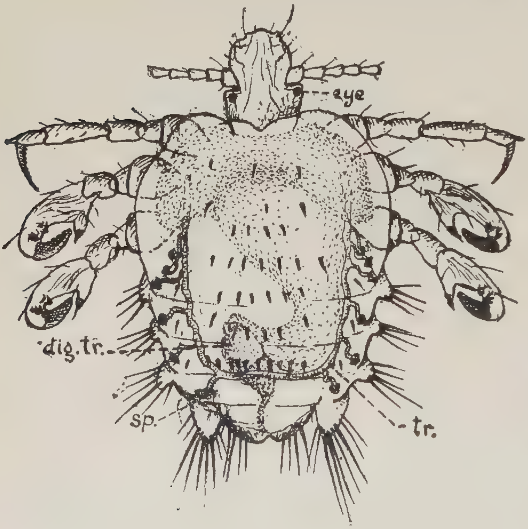

Fig. 222. Crab louse, *Phthirus pubis*, ♀. × 35.

The females produce from ten to 15 eggs and glue them, one at a time, to the coarse hairs among which they live. A number of eggs may be glued to a single hair, and often at some distance from the skin. The eggs hatch in six or seven days, and the young become sexually mature in about 15 days. This species, even under favorable conditions, will live apart from its host only ten or 12 hours. The eggs are said not to develop except at temperatures between 68° F. and 86° F., which are approximately the temperatures to which eggs attached to hairs beneath the clothing would be exposed in cool climates.

Lice and Disease

The rôle of lice in the spread of disease has long been suspected in an indefinite and uncertain way. Only recently, and at the cost of the lives of several great investigators, has the whole portentous truth regarding the transmission by them of typhus and relapsing fever been brought to light. Foremost among the investigators of louse-borne diseases stands the name of Nicolle and his associates, who in 1909 proved that typhus fever could be transmitted by the body louse, and in 1913 that the Algerian type of relapsing fever could be transmitted likewise. Two American investigators, Ricketts and Wilder, working independently of the French workers, proved in 1910 that the body louse was instrumental in transmitting typhus (tarbardillo) in Mexico, and in 1912 Anderson and Goldberger showed that the head louse could also transmit it. In 1918 an American commission under Dr. R. P. Strong, and a British committee under Sir David Bruce and Major Byam, working under field conditions on the war front in France, demonstrated that trench fever is a louse-borne disease.

Typhus and other Rickettsia Diseases. — Typhus is normally transmitted only by body and head lice; there is no evidence that the crab louse can transmit it. The epidemiology shows that body lice are primarily involved, but head lice can also acquire the infection under experimental conditions. It is probable that it is less frequently involved in typhus epidemics mainly because of its less frequent transfer from person to person. Typhus epidemics occur most commonly where people are crowded together under unsanitary conditions, especially in cold weather, as in jails, barracks, military and laborers' camps, etc., where the lice nightly migrate from one pile of dirty clothing to another.

The causative organism of typhus, *Rickettsia prowazeki*, occurs abundantly in the human and also in the epithelial cells of the gut of infected lice. According to investigations by Sergent, Foley, and Vialatte the lice do not become infected from feeding on patients during the incubation period of the disease; during the first days after the onset only a small percentage become infected, but with the progress of the disease the frequency of infection in lice after biting the patient steadily increases until, between the 20th and 25th days the majority become infected. It is also stated that eggs from infected lice can cause infection if inoculated, but Nicolle has failed to produce infection by means of young lice from infected parents, and thinks the eggs were merely contaminated by feces of the parents. Not all lice biting typhus patients become infected, and the typhus organisms eventually destroy the infected lice, which is unusual in an intermediate host. Rickettsias have not been observed in the esophagus or salivary glands of lice but are present in the feces. It is stated that lice can transmit the infection directly by biting, but it is likely that crushing of infected lice, or contamination of the bites with the feces, is the usual if not the sole method of transmission. Lice do not ordinarily become infective until the eighth, and usually the ninth or tenth day, after an infective feed. Further details concerning typhus and its causative agent, *Rickettsia prowazeki*, will be found on p. 188.

Epidemics of typhus are associated with a huddling together of people in warm, poorly-ventilated living quarters, especially in cold weather, partly because such conditions favor the multiplication and interchange of lice, and partly, perhaps, because the unhygienic conditions tend to lower resistance to disease. It is significant, however, that even individuals such as nurses and doctors, who come in intimate contact with lousy individuals under unhygienic conditions, even though they themselves live under ideal conditions, are not spared when typhus breaks out. Typhus has followed in the wake of nearly every army which has ever been assembled, since the conditions incident to warfare, breaking down normal conditions of cleanliness and sanitation, always favor the multiplication and spread of lice. During the great war typhus was very largely kept under control by the armies of Britain, France, Germany and America due to the intensive anti-louse measures which were enforced, to as great an extent as was possible, by these nations. The less scientific and less cleanly nations have suffered enormous losses. An epidemic began in Serbia in January, 1915, among some Austrian prisoners who were allowed to disperse all over the country. The disease spread with them, and for a time raged almost at will in that war-stricken country. The majority of the small number of Serbian doctors were affected, no sanitary measures for the suppression of lice were understood or enforced, and no adequate accommodations for the sick could be provided. The epidemic continued to rise, and reached its height in April, when there were estimated to be 9000 deaths per day. It was largely through the heroic efforts of an American Red Cross expedition that the epidemic was finally checked, after having destroyed over 150,000 people. In December, 1916, another epidemic was reported to be raging in Syria with over 1000 deaths per day. Milder epidemics occurred in Austria, Bulgaria and Russia, all countries where science and cleanliness have not been worshipped as they have in the greater nations of Europe. Mexico suffers also; in December, 1915, 11,000 cases of typhus were reported in Mexico City and its environs. Since the war, with the return of more normal conditions of sanitation and a great reduction in the intermixing of clean and unclean people, typhus has not caused such sweeping epidemics, but sporadic cases and small local epidemics constantly occur. This is due to the fact that in civilized countries, which are those in which body lice primarily occur (since in the tropics it is often either too hot or insufficient clothes are worn), unclean, lousy people are nowadays in the minority, and in communities of such people a high percentage soon become immune as the result of previous infections.

Soon after the outbreak of the great war a previously unknown disease, trench fever, made its appearance. Between 1916 and 1918 it assumed such proportions as to have caused more sickness among troops in France than any other infectious disease. In 1918 an American and a British commission, working under war conditions, demonstrated that the disease was, ordinarily at least, transmitted by lice; their work is a brilliant piece of medical research carried out successfully in spite of adverse conditions. The louse can transmit the disease by its bite alone or by infection of abraded skin by the excrement. Evidence has since been adduced to show that the disease is probably caused by a Rickettsia, *R. quintana*, which is found in the lumen, but not in the cells, of the intestine of infected lice. A related disease, known as Volhynian or five-day fever, is believed also to be a Rickettsia disease transmitted by lice, and may be identical with trench fever. The origin of trench fever is an interesting question. Many lice which have had no opportunity to feed on cases of either typhus or trench fever harbor a non-pathogenic Rickettsia which has been called *R. pediculi*. Among a people who are constantly infested by lice it is conceivable that such an organism would have little opportunity to develop into a virulent strain, since the majority of the people would be immunized by repeated injections of the non-virulent strains during the early years of life. The organism, even if it did occasionally develop mild virulence would have difficulty in building it up on account of the habitual feeding of the lice harboring them on immune people. Under such conditions only sporadic cases or at most local mild epidemics would be likely to occur. With the conditions existing in war time, with opportunity of lice to infest vast numbers of people who had never before been infested and who could have no immunity to *R. pediculi* infection, it is conceivable that a virulent strain could be built up in such individuals by repeated transmission to non-immunes, which under war conditions would then certainly be able to assume epidemic proportions. This is, of course, a purely hypothetical explanation. It is significant that since the close of the war little more has been heard of trench fever. (See p. 188.)

Lice and Relapsing Fever. — The rôle of lice in the transmission of the European and North African form of relapsing fever has long been suspected but was not proved until 1913, when Nicolle and his fellow-workers scientifically demonstrated it in Tunis and Algeria. Noting that the louse was the only constant factor affecting the occurrence of the disease, these French workers undertook extensive experiments which resulted in proving that the body louse, and probably also the head louse, serves as a medium for the development of the spirochætes of relapsing fever, and that these insects transmit the disease not by biting but by inoculation of the wounds which they make with the infected contents of their bodies when crushed. Details of the development of the spirochætes in the lice are given in Chapter IV, p. 55.

Nicolle and his associates also showed that sometimes, at least, the spirochætes, possibly in the granule stage, are hereditarily transmitted through the eggs to the young of the next generation, as is the case with relapsing fever parasites in ticks. Experiments on the transmission of the relapsing fever of Algeria with other parasites such as bedbugs, fleas, biting flies and ticks were negative. The epidemiology in Europe at times suggests that bedbugs, too, may be involved (see p. 448), but there is little evidence in support of this. All the positive evidence at present supports the view that the various strains of relapsing fever spirochætes develop either in ticks of the genus *Ornithodoros* or in lice, rarely in both. Lice are involved in the transmission of the *recurrentis* strain of Europe and the *berbera* strain of North Africa as already noted, and also the *carteri* strain in Central and Southern India (but not the form found in northwest India), the *novyi* strain in America, and also strains occurring in Persia, the Anglo-Egyptian Sudan, and in West Africa north and west of the Cameroons.

Being transmitted by lice, relapsing fever shows the same peculiarities of occurrence as does typhus; epidemics always rage fiercest in winter, and usually break out during war times. Serbia, which was so stricken by typhus, was held in the grip of an epidemic of relapsing fever earlier in the great war.

Lice and Other Diseases. — Lice may also serve as mechanical transmitters of still other diseases. The bacilli of bubonic plague have been found alive in both body lice and head lice taken from victims of the disease, and both this species and the body louse have been experimentally proved to be able to transmit plague from rodent to rodent in Java. De Raadt in Java infected rodents with plague by injecting them with ground bodies of head lice taken from plague patients. The practice among some natives of killing lice by mashing them against the head of the host, accompanied by the frequent scratching due to irritation from bites, may well be a frequent cause of plague infection if there has been any opportunity for the lice to migrate from an infected to a healthy person.

Most bacterial diseases are not transmitted by lice, except possibly immediately after an infective feed, since few bacteria survive in the digestive tracts of these insects. The anti-bacterial substance present in the guts of most insects is active in lice, the gut contents of which are nearly always bacteria-free.

Lice have been suggested as possible transmitters of *Leishmania* diseases, and this idea was supported by some experiments of Fantham and Porter who reported having infected mice from herpetomonad flagellates in lice, but other workers have failed to confirm the results of these workers. There is no epidemiological evidence for the transmission of either kala-azar or Oriental sore by lice.

Lice are said not to harbor the spirochætes of infectious jaundice as do bedbugs. Theoretically they might transmit syphilis or yaws, but there is no evidence to support this idea, and the epidemiology does not suggest it. Lice have been suspected in the case of various other diseases also, just as bedbugs have, but there is no scientific evidence to support the suspicions.

Prevention and Remedies. — The prevention of lousiness consists primarily in personal cleanliness. However, no amount of personal hygiene and cleanliness will prevent temporary lousiness if there is association with unclean and careless companions. Lousiness and human wretchedness and degradation have always been companions, but this does not imply that lice have any inherent abhorrence of a clean body if they can get access to it. From the nature of their habitats the common modes of infection of the three different species of human lice vary somewhat. Any of them will spread by contact or close association but each has its own special means of finding new hosts. The head louse depends largely for distribution on a promiscuous use of combs and brushes or borrowed hats and caps, and on the free-for-all trying on of head gear in haberdasheries and millinery shops. The body louse is dispersed by clothing and bed linen and finds fresh hunting grounds by night migrations from one pile of clothes to another. The crab louse frequently utilizes public toilets for dissemination and is commonly spread by promiscuous sexual intercourse. Where men are crowded together in prisons or war camps lousiness is almost sure to develop unless particularly guarded against, since some uncleanly persons are nearly always in the aggregation, and conditions are such that the infestation is given every opportunity to spread. There are, however, many ways in which lice may be dispersed among clean people in ordinary life. Stiles reports a case where a large number of girls in a fashionable boarding house in eastern United States developed lousiness shortly after traveling from Chicago to New York in a Pullman sleeper. In places where negresses or dirty natives do much of the laundering the family wash is a common source of infestation. Closely packed street cars, school cloak rooms, gymnasium lockers, unclean rooming houses — all these and many other means may serve to start a new colony of lice.

Perfect cleanliness will usually result in their quick elimination. A shampoo with warm water and soap, frequent baths, clean underclothes, pressed suits, and other items of personal care are inimical to the welfare of the unwelcome visitors. Certain remedies are, however, useful in the quick destruction of these pests. Head lice can best be destroyed by a thorough washing of the head with a two per cent carbolic acid solution or a kerosene emulsion (equal parts kerosene and olive oil or vinegar). An ointment made up of oil of lemon grass, pennyroyal and eucalyptus, 3 parts each, and powdered naphthaline 1 part, mixed with vaseline in the proportion of 2 cc. to 8 gr. of vaseline, is said to destroy both lice and their eggs. When one of these remedies has been thoroughly rubbed into the hair the head should be covered with a cloth. After several hours the ointment is washed off in warm water and soap and the dead lice removed with a fine-tooth comb. In long hair this treatment is applied by having the patient lie down with the hair hanging over the edge of a bed into a pan of the carbolic solution or kerosene emulsion, the hair being sluiced backward and forward for ten minutes until thoroughly saturated. The treatment may have to be repeated after about ten days to destroy lice which have hatched in the meantime, but usually the eggs are destroyed as well as the adult lice. In men in camps or barracks a close clipping of the hair, a time-honored custom, is one of the best methods of getting rid of head lice. Crab lice can be destroyed best by the use of mercurial ointment applied to the infected parts, accompanied by washing with soft soap and warm water. A close clipping of the hair in the infested regions is the safest and quickest method of getting rid of the nits. When the eye lashes are infested the lids can be washed with 5% cocaine to cause the lice to release their holds, and they can be brushed out after about ten minutes. A repetition is necessary after the eggs have hatched.

Eradication of body lice is in some respects simpler than that of other lice, since it is the clothes instead of the body which are to be treated. An ingenious tramp in France was found ridding himself of lice by divesting himself of his clothing and laying it on the nest of black ants. When the ants ceased to take an interest in the clothing he shook them out and proceeded on his way, assured by previous experience that he would have no further troubles from lice for a while.

Much work has been done since the outbreak of the war in Europe on testing the effect of various chemicals and methods of treatment on lice. This problem is recognized as one of the most important minor considerations in war.

The methods employed in ridding clothing of body lice and their eggs consist of the application of heat or of chemical disinfectants or insecticides.

Heat may be applied in the form of boiling water, steam or dry heat. Clothes which can be boiled without injuring them are most easily and surely disinfested by immersion in hot water during the process of laundering. An immersion of 10 seconds in water of 160° F. is sufficient to kill both lice and nits, and they are killed instantly in boiling water. Many devices have been suggested for the delousing of clothing by means of steam. It is unnecessary to use steam under pressure or prolonged exposure to live steam as in the case of bacterial disinfection; it is only necessary to insure that the steam be applied in such a manner that all parts of the clothing are actually heated to about 170° F., or even to as low a temperature as 130° if applied for as long as 30 minutes. This can be done by as simple a device as the " Serbian barrel." Nuttall (1918) states that " a 60-gallon barrel is capable of coping with 4 soldiers' kits or 7 blankets at a time. The barrel having its top and bottom knocked out is provided with a grated wooden bottom and a flat wooden lid which can be weighted if necessary with stones." The barrel may be placed over a circular boiler, or steam, led into the top of a barrel (with impervious bottom), percolates through it, and the condensed water is drawn off by a spigot at the bottom. Half an hour to an hour's steaming is advised. Converted railway cars, boxes, rooms and many other containers in which clothing can be hung can similarly be used with steam, generated from a locomotive or heating plant, turned into them.

Woolens shrink when exposed to moist heat at high temperatures and most laundries wash them at temperatures too low to destroy lice and nits. They can, however, be washed at 120° F. for 15 minutes and then dry heated in a hot air " tumbler " at 150° to 170° F. for 10 or 15 minutes.

When delousing alone is desired, dry hot air is preferable since it can be applied to many more objects without injury, costs less, and can handle a larger amount of goods. Hot air penetrates rapidly among loosely hung clothing between which it circulates, but stagnant air penetrates very slowly; fans or other devices for insuring circulation are necessary. The simple process of ironing clothes with a hot iron, if care is taken to run the iron along all the seams, is a method which gives good results if done thoroughly.

Many chemicals can be used for delousing, either in the form of gases (fumigants) or solutions. The ordinary methods of fumigation described on pp. 456 to 460 are all effective in destroying lice, but other methods can also be used. The vapor of many essential oils is injurious, and the mixture of oil of lemon grass, pennyroyal, eucalyptus and naphthaline described above is said to be effective if used at the rate of 5 cc. per cubic meter with an exposure of 20 minutes at a temperature of 105° to 112° F. An atmosphere saturated with naphthaline vapor alone is also destructive in 15 minutes at similar temperatures. Vapor of ammonia, chloropicrin, chloroform, carbon tetrachloride, carbon bisulphide, etc., are also lethal to the lice and nits. Immersion of clothing in solutions of mercuric bichloride (1–1000); a 10% solution of cresol (35%), soap (65%) and kerosene; 1.5% cresol solution for one hour; or mixtures of kerosene and vinegar have been recommended, and are no doubt all effective, but plain hot water is cheaper and easier to use.

Preventive measures against lice, simple as they are under ordinary conditions, often constitute a very difficult problem, especially in army camps. Common methods employed are the treatment of the clothes with odorous or poisonous substances, the use of underclothes with smooth inner surface, such as silk or oil cloth, to which lice cannot attach their eggs, or the dusting of naphthaline powder into the shoes, stockings and underwear. A substance which was found most efficient during the war, and was used extensively on the western front in France is the now famous "NCI," a powder consisting of 96% commercial naphthaline with 2% creosote added to increase the toxicity and to give lasting qualities and 2% iodoform to increase the adhesiveness of the powder when dusted on the inside of the clothing. The shepherd people of the Carpathians are said to protect themselves against lice by saturating their underclothes in melted butter which prevents the lice from fastening their eggs to the fibers of the clothes, and probably the fatty acids of rancid butter are also directly deleterious to the pests. In any methods of delousing on a large scale some system is important whereby the re-infestation from others of deloused clothing or individuals can be prevented, and the delousing establishment should have a "clean" side and an "unclean" side, with precautions to prevent the carrying of lice by goods or personnel from one side to the other. During the war there were huge delousing stations established by the Germans on their Eastern front, where they were in contact with peoples among whom lice and typhus were rife; some of these were capable of delousing, and incidentally cleaning up generally, as high as 12,000 men every 24 hours. Similar establishments were operated on an even larger scale at Brest and Bordeaux for the delousing of American troops before they were allowed to embark for the United States. The methods employed would have been even more effective than they were had it not been for the non-coöperation of Russian prisoners, who by all sorts of subterfuges tried to avoid being "laundered."

Many European peoples hang little sachets or pieces of cloth between the underclothes and the body, saturating them at intervals with various essential oils or powders containing such substances as naphthaline and sulphur. Though these "amulets" afford some protection if frequently renewed, they are not very efficient, and cannot be relied upon to protect one from louse-borne diseases.

CHAPTER XXV

FLEAS

David Harum says, " A reasonable amount of fleas is good for a dog. They keep him from broodin' on bein' a dog." A goodly supply of fleas might likewise keep man from brooding over anything deeper than the presence of these fleas, but in many cases this in itself is a rather serious thing to brood over. Not only are fleas very annoying pests and a common cause of insomnia, but they may also serve as the disseminators of a number of serious human diseases, among which the terrible bubonic plague stands foremost.

General Structure. — Fleas are insects which are believed by most entomologists to be more or less distantly related to the Diptera or two-winged flies, but which have become so specialized by their particular mode of life as external parasites as to necessitate their segregation into a distinct order of their own, the Siphonaptera. Their bodies are ordinarily much compressed to facilitate gliding between the hairs or feathers of their hosts. The head is broadly joined to the thorax, which is relatively small. The abdomen is large and much compressed from side to side; it consists of ten segments, the first seven of which are simple rings, each protected by two horny plates, a dorsal " tergum " and a ventral " sternum " (Fig. 223). The last three segments are modified differently in the male and female in connection with the sexual organs. In both sexes the " tergum " of the ninth segment has a pitted area covered with little bristles which is called the pygidium, and is probably sensory in function. All parts of the body are furnished with backward-

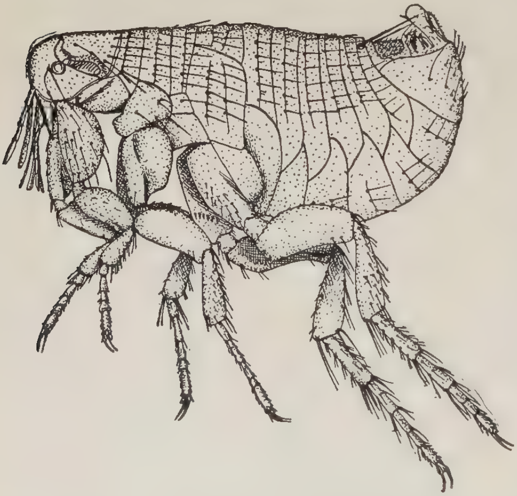

FIG. 223. The Indian rat flea, *Xenopsylla cheopis*, male. × 50. (After Jordan and Rothschild.)

projecting bristles and spines which aid the flea in forcing his way between dense hairs and in preventing him from slipping backward. The efficiency of these spines is apparent when one attempts to hold a flea between his fingers. Many fleas have specially developed, thick, heavy spines arranged in rows suggestive of the teeth of combs and therefore known as ctenidia or " combs " (Fig. 226). Such a comb may be present either along the ventral margin of the head or along the hind edge of the pronotum (the dorsal plate covering the first segment of the thorax) or in both places. The presence or absence of these combs and the number of teeth in them is of considerable use in identification of species.

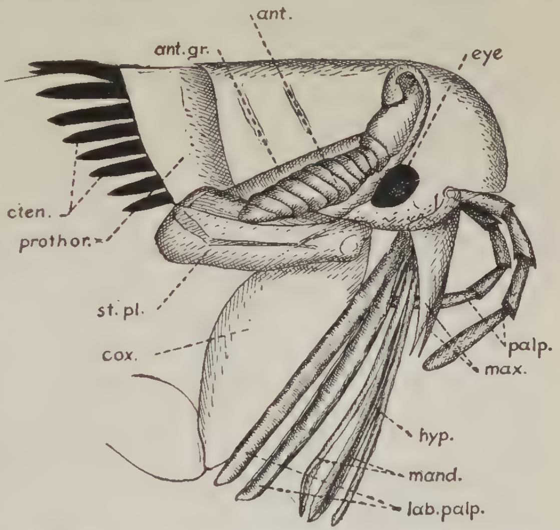

FIG. 224. Head and mouthparts of a flea (squirrel flea, *Ceratophyllus fasciatus*); *ant.*, antenna; *ant. gr.*, antennal groove; *cox.*, coxa of 1st leg; *cten.*, ctenidium; *hyp.*, hypopharynx; *lab. palp.*, labial palpi, which together form a tube for protecting the lancets; *mand.*, mandibles; *max.*, maxilla; *palp.*, maxillary palpi; *prothor.*, prothorax; *st. pl.*, sternal plate of skeleton with which leg is articulated.

The legs of fleas are very long and powerful, and at first glance seem to possess one more segment than do the legs of other insects. They really consist of the usual number of segments, however, but are peculiar in the enormous development of the first segments of the legs (coxæ), which in most insects are quite insignificant (Fig. 224). The shape of the sternal plate to which the coxæ are attached is suggestive of still another segment. The great development of the coxæ as well as of the other segments of the leg gives unusual springiness and consequently enormous jumping power. The human flea, *Pulex irritans*, has been observed by Mitzmain to jump 13 inches horizontally and seven and three-fourths inches vertically. An equivalent jump for a man of average height would be over 450 feet horizontally and over 275 feet vertically! The jumping power must overcome to some extent the disadvantage of winglessness and render migration from host to host comparatively easy. All the legs are furnished with rows of stout spines and are armed at the tip with a pair of large stout claws.

Eyes are present in some species of fleas but not in others. The antennæ are short and club-shaped, and when not in use are folded back into special grooves for them on the sides of the head (Fig. 224, *ant. gr.*). The mouthparts (Fig. 224) are fitted for piercing and sucking. In the normal resting position they appear to consist of a long jointed proboscis, blunt at the tip, with a pair of stout, pointed pyramidal organs at either side at the base, used for holding the flea in position while feeding. These structures are the maxillæ and each is provided with a stout four-segmented palpus, which might easily be mistaken for an antenna. The proboscis really consists of a pair of segmented gouge-shaped structures, the labial palpi, which fit together to form a more or less perfect tube, in which lie three piercing organs. The latter consist of a pair of thin bladelike mandibles serrated on each edge, curved at the tip, and provided with a longitudinal groove, and a single bristle-like organ, the labrum-epipharynx. The serrated mandibles are the piercing and cutting weapons, and are used in a saw-like manner. As these organs are sunk into the flesh of the host the labial palpi bend back like a bow under the flea's head. The two grooved mandibles, placed in apposition, form a tube for the outflow of saliva, while the labrum-epipharynx, which is also grooved, forms a tube with the mandibles for the inflow of blood. The digestive tract is provided with a pharynx which acts like a suction pump, and a very large and distensible stomach.

The male external genital organs, consisting of complicated claspers and other organs, as well as the pygidium, are modified parts of the ninth segment of the abdomen. The details of structure of these parts are often of great taxonomic value in male fleas. In the females the terminal segments of the abdomen are compressed and inconspicuous. In this sex a taxonomic character of great importance is the form of the spermatheca, which is chitinized and easily seen inside the abdomen in cleared specimens.

Classification. — Several hundreds of species of fleas have been described, and more are constantly being discovered. By some authors the order Siphonaptera is divided into two suborders, the Fracticipita, or broken-headed fleas, which have the head divided into an anterior and posterior part by a movable joint, and the Integricipita, which have unjointed heads (cf. Figs. 226 *A*, *B* and *C*). It happens that nearly all of the important fleas from the standpoint of human annoyance and disease belong to the latter group. The division of fleas into families is a matter on which few entomologists yet agree. One family, the Echidnophagidæ, can be definitely recognized; it includes the chigger-flea and "stick-tight" flea, which are distinguished by the much shortened thorax which appears as if telescoped between the head and abdomen, by the slender anterior and middle legs, and by the feeble labial palpi of only three segments. The division of other fleas into separate families is not yet practical.

The differentiation of genera of fleas is based largely on the presence or absence of ctenidia on the head or on the pronotum, the number of rows of bristles on the abdominal segments, the presence or absence of eyes, the form of the antennæ, and many minor characters of chætotaxy and form of certain plates of head or thorax. The species are distinguished by very minute characters in many cases, and even experts may disagree on identifications. Most species of fleas, however, are normally fairly

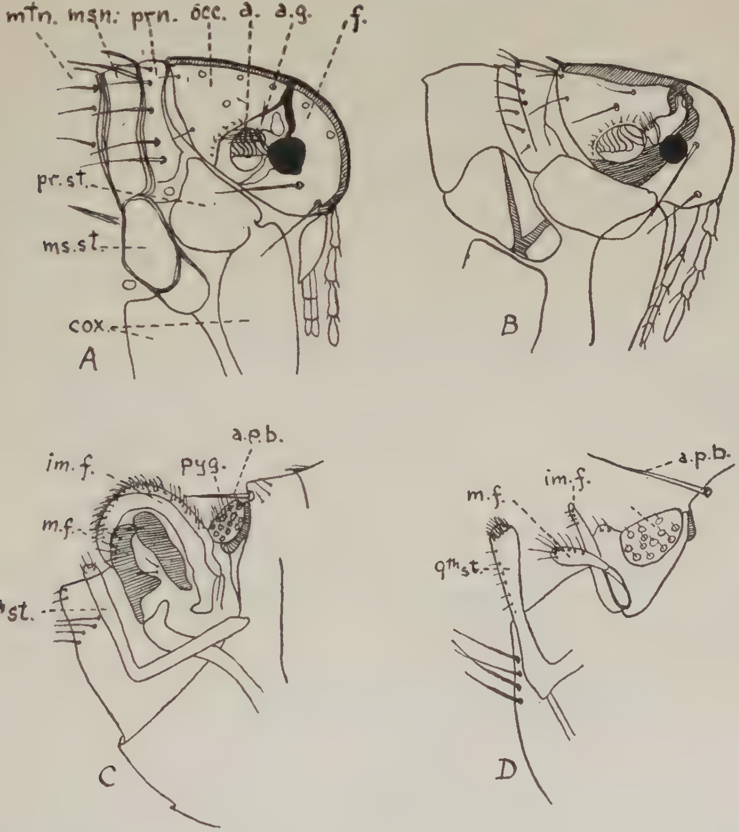

FIG. 225. Heads and posterior part of male abdomen of *Pulex irritans* (*A* and *C*) and *Xenopsylla cheopis* (*B* and *D*), *a.*, antenna, *a. g.*, antennal groove; *a. p. b.*, antepygidial bristle; *cox.*, coxæ; *f.*, frons; *im. f.*, immovable finger process of clasper; *m. f.*, movable finger processes of clasper; *msm.*, mesonotum; *ms t.*, mesosternum; *mtn.*, metanotum; *occ.*, occiput; *prn.*, pronotum; *pr. st.*, prosternum; *pyg.*, pygidium; 9*th st.*, 9th sternite. (After Fox.)

closely confined to particular kinds of hosts, only a few species being able to thrive on a variety of different hosts. If the host and geographic locality is known the number of species which have to be considered in identifying a flea is comparatively limited and a fairly close identification can usually be made of fleas found in houses by the presence or absence of genal and pronotal ctenidia and the number of spines in them. The human flea, *Pulex irritans*, (Fig. 225 *A* and *C*) and the rat fleas of the genus *Xenopsylla* (Figs. 223, 225 *B* and *D*), which are of particular importance in connection with the transmission of plague, have no combs; the common rat fleas of temperate climates (*Ceratophyllus*) (Figs. 224 and 226*C*) have only the pronotal comb; the cat and dog fleas (*Ctenocephalus*), (Fig. 226*A*) have a pronotal comb and a horizontal genal comb; and the common mouse flea, *Ctenopsylla segnis* (=*Leptopsylla musculi*), (Fig. 226*B*) has a pronotal comb and a short vertical genal comb of only four spines.

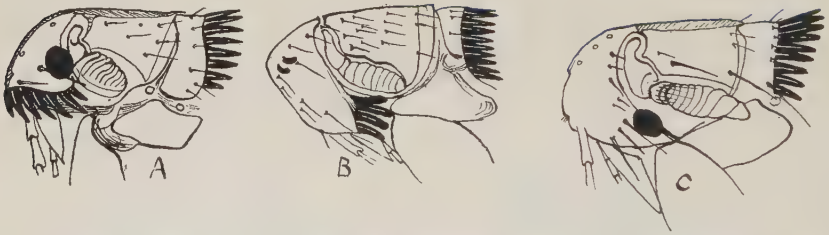

Fig. 226. Heads of fleas, showing arrangement of ctenidia. *A*, *Ctenocephalus canis;* *B*, *Ctenopsylla segnis* (=*Leptopsylla musculi*); *C*, *Ceratophyllus fasciatus*. *A* and *C* belong to the Integricipita, while *B* belongs to the Fracticipita; note the joint over the head above the antennal groove. (After Fox.)

Life History and Habits. — Most fleas are neither as strictly host parasites as are lice or as strictly nest parasites as are bedbugs. The nests or lairs of the host are the homes of the eggs, larvæ and pupæ, and frequently adults are found in them too, but these are often either newly emerged fleas or fleas which have dropped off to deposit eggs. According to some investigators some rodent fleas are more frequently found in the nests than in the fur of the host, but this appears to require confirmation, although it is true of some bird fleas. The fact that fleas leave the body of a dead host as soon as it becomes cold, and often show a preference for certain parts of the body, indicate that these insects as adults are normally body parasites. The nests or dens are, however, the normal breeding places, and it is significant that those mammals which have no permanent habitations, such as monkeys and deer, are nearly free from fleas, although they seldom lack for lice. Flea larvæ thrive on blood, and in some cases, *e.g. Ceratophyllus fasciatus*, are said to require it, yet they have no means of their own for obtaining it and the parents have to provide it in a semi-digested condition in their feces. The larvæ of *Xenopsylla cheopis* is said not to require blood. It is evident that the tendency for fleas to leave their hosts for egg laying mainly in the nests is a wise provision of nature for the satisfactory nourishment of the larvæ. Possibly the warmth generated by the host in its nest while sleeping, or some odors connected with it, indicate to the flea that the time and place is right for an excursion off the host.

The eggs of fleas are oval, pearly-white objects of relatively large size, sometimes one-third the length of the parent flea. Except in the case of the chiggers they are laid singly, (frequently?) being dropped at random. The human flea, for instance, drops its eggs in the dust and débris in cracks in floors, under carpets, etc., whereas the fleas of most mammals lay their eggs in the nests or dens of their hosts or else deposit them loosely in the fur of the animals, whence they drop off when the animal shakes himself or prepares to sleep. In *Xenopsylla* the eggs are viscid and adhere to débris, and are not laid in the fur of the host. The time required for the eggs to reach the hatching stage varies with the species, and with climatic conditions, from two or three days to over two weeks. The eggs are relatively least susceptible to unfavorable environmental conditions. Eggs of *Ceratophyllus fasciatus* will hatch at temperatures as low as 41° F., but those of *Pulex* and *Xenopsylla cheopis* require higher temperatures and will hatch even at 93° F. The most favorable conditions for the development of most species are temperatures between 65° and 80° and a humidity of about 70%. The higher the temperature the greater the humidity required. In the nests and holes where fleas breed, however, favorable conditions of temperature and moisture may exist even when conditions in the open are highly unfavorable.

The larvæ (Fig. 227) are tiny cylindrical maggot-like creatures with neither legs nor eyes. They have small brown heads and whitish bodies composed of 13 visible segments and a terminal hidden one, which are provided with rather sparse bristly hairs to aid in crawling. The last segment is terminated by a pair of tiny hooks.

The larvæ squirm about actively in the dirt or débris in which they hatched, avoiding light and feeding upon what bits of organic matter they can find, such as mouse pills, crumbs, hairs, epidermal scales from their hosts and the excrement of adult fleas. Some species, if not all, devour their shed skins after moulting. According to Bacot and Ridewood, who have recently made observations on the larvæ of a number of species of fleas, the larvæ become very excited and impatient when disturbed. They sometimes lie quiet, coiled like a watch spring, for repose or concealment, but when about to moult they stretch out at full length. They crawl by alternately expanding and contracting the body like an earthworm, first securing a hold with the hooks at the posterior tip of the body, then with the head which is bent under to hook over some irregularity on the surface. The duration of the larval stage varies with the temperature and humidity and to some extent also with the species. Under favorable conditions, *i.e.*, at relatively low temperatures and high humidity and with plenty of food, the larvæ of some species pass through their two moults and enter the pupal stage in a week, whereas under unfavorable conditions the duration of the larval existence may be drawn out to over three months.

When ready to undergo their transformation into adults, the larvæ spin little silken cocoons which are somewhat viscid, so that particles of dust and lint readily adhere to them and give them a dirty, dingy appearance (Fig. 227). According to Lyon the adult insects may emerge from the cocoons of the cat flea, *Ctenocephalus felis*, in from 2 to 14 days, but in most species at least a week is required for the transformation to take place, and this time may be greatly increased by unfavorable climatic conditions. Strickland, in his work on the rat flea of England, *Ceratophyllus fasciatus*, found that the average pupal existence was 17 days and was extended to four months or more by low temperatures, the fully formed adult insect remaining dormant within the cocoon until exposed to a temperature of about 70° F. There is much probability that the winter in temperate climates and the hot dry season in tropical climates is tided over by fleas in the cocoon, the emergence of the adults coinciding with the advent of moderately high temperatures and humidity.

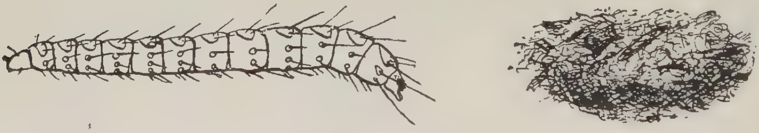

Fig. 227. Developmental stages of fleas. Left, larva of *Xenopsylla cheopis* (after Bacot and Ridewood); right, cocoon of *Pulex irritans*. × 12.

The adult fleas, according to Strickland's work on the rat flea, do not become sexually mature for some days after they escape from the cocoon, and copulation does not occur until this time, nor, in the case of the rat flea, until after a feed of rat's blood, the latter apparently acting as a stimulus to reproduction. Soon after copulation the eggs begin to be laid.

In the dog flea, *Ctenocephalus canis*, the entire cycle from egg to adult is said to be passed through in a minimum of two weeks, in the human flea, *Pulex irritans*, in 19 days (in southern Europe) and in *Ceratophyllus* in about three weeks. Ordinarily, however, the life cycles occupy a considerably longer time, the average being from one to three months. Under tropical conditions, as for instance in Colombo, according to Hirst, the eggs of *Xenopsylla* hatch in from 4 to 5 days, pupate about 10 to 13 days after the eggs are laid, and emerge as adults after 8 to 16 days of pupation, the entire cycle occupying from 18 to 37 days, averaging about 25 days.

The length of life of adult fleas depends largely on food supply, temperature and humidity. At low temperatures (60° F.) well-fed rat fleas will live for 18 months, according to Strickland. Bacot has kept *Pulex irritans* alive for a similar length of time. In the absence of a host, at low temperatures most fleas can live for from 1 to 2 years. Under only moderately unfavorable conditions, however, the powers of endurance of fleas are slight when kept without food. Under tropical conditions *Xenopsylla cheopis* will survive only about two weeks. No breeding takes place without blood meals; abundance of food affects the number but not the fertility of eggs. In Southeast Russia and Turkestan *Ceratophyllus tesquorum* will survive for months in very cold weather in the burrows of ground squirrels (susliks), and this is probably true of many other rodent fleas. The optimum climatic conditions and normal length of life probably vary a great deal with different species. Most of the species of *Ceratophyllus*, and also *Pulex irritans*, are fleas of temperate or cold climates, while those of *Xenopsylla* are characteristic of hot climates.

Unlike most blood-sucking insects, fleas usually feed at frequent intervals, usually at least once a day, and sometimes much oftener than this. The frequent biting is due to the fact that fleas are very easily disturbed while feeding and seldom complete a meal at one bite. Moreover, the capacity of the stomach is not so great as in many other blood-sucking insects. Fleas frequently feed even when the digestive tract is already well filled, and may pass practically unaltered blood in their feces to be utilized, second-hand, by the larvæ.

Fleas and Disease. — Like most other blood-sucking parasites, fleas are intimately connected with the transmission of disease. The most serious charge against them is the dissemination of bubonic plague, which alone is sufficient to rank fleas among the most important insect enemies of man. Fleas are also important transmitters of tularemia among rodents; they serve as intermediate hosts of certain tapeworms; and they have been suspected in connection with other diseases, especially the Mediterranean type of leishmaniasis.

Fleas and Plague. — Bubonic plague ranks as a human scourge with such diseases as smallpox and leprosy. In fact, few diseases have ever ravaged the human race with more terrible destructiveness than plague when it breaks forth as an epidemic and becomes rampant. It is estimated that in the epidemic of the 14th century in Europe one-fourth of the population of that continent, or 25 million people, died of the disease. Superstition and unreasoning terror led to horrible persecution and torture of innocent people who were supposed to cause the plague. At present the disease is largely confined to tropical countries, and is especially prevalent in India, where an average of over half a million deaths a year are caused by it. The practical disappearance of plague from Europe is thought by some authors to be associated with a change in the rat fauna of Europe, the domestic and gregarious black rat, *Rattus rattus*, being replaced by the wilder and more scattered brown rat, *Rattus norvegicus*. The disease, however, has often been introduced from the tropics into other countries, and, while it does not usually assume epidemic proportions, it often smolders on for a long time in an endemic condition, establishing itself in local rodents and from time to time causing human outbreaks. Serious endemic foci of wide extent have been established in Mongolia, Central Asia and southeast Russia, in the Orange Free State in South Africa, and in California. More local and usually temporary foci have been established in nearly all the important seaports in the world. In America outbreaks have occurred within recent years in many ports on the Gulf of Mexico, and Sydney, Australia, has also suffered. There is constant danger of fresh introductions in seaports wherever the strictest preventive regulations are not enforced. With modern knowledge of the epidemiology of the disease, and intelligent and active measures against it, there is no danger that epidemics such as once ravaged Europe will be seen again, but once the disease has obtained a foothold the fight is a strenuous and expensive one.

The steps which have made possible an intelligent fight against plague were the discovery of the plague germ, *Bacillus* (*Pasteurella*) *pestis*, by Yersin in 1894, the establishment of the identity of the disease with that of rats by the same worker, the discovery of the multiplication of the plague germs in the gut of rat fleas, *Xenopsylla cheopis*, by Liston in 1905, and finally conclusive experimental proof by the British Plague Commission in India in 1906 that the rat flea was the principal means of transmission of the bubonic form of the disease.

The usual mechanism of transmission was made clear by the work of Bacot and Martin in 1914. They observed that the Indian rat flea, *Xenopsylla cheopis*, after feeding on an infected animal, often had its digestive tract completely blocked by solid growths of plague organisms. Such " blocked " fleas are unable to ingest more blood and in attempting to do so, since the normal action of the valves of the pharynx is impaired, they regurgitate great quantities of plague germs into their victims. Fleas may remain infective for a long time, but many fleas die when " blocked," especially in hot or dry weather, since they are unable to overcome the effects of desiccation by imbibing fresh blood.

It is now known that the spread of plague depends on the complicated interaction of a number of factors which have to do with each of the three main organisms involved — rats or other susceptible rodents, fleas, and plague germs. Climate plays an important part; plague epidemics occur only when the mean temperature lies between 58° and 80° F., although epizoötics among wild rodents, with sporadic human cases, may occur at mean temperatures down to 50°. The epidemics are further limited by humidity, and the drying power of the air must not be greater than that represented by a vapor pressure deficiency of 7.5 mm. Rodents affect the epidemiology by their species, abundance, habits, plague susceptibility and seasonal characteristics. The black rat, *Rattus rattus*, being the most domestic species and the main host of *Xenopsylla cheopis*, is the species most frequently associated with plague outbreaks; plague also establishes itself readily in brown rats, *Rattus norvegicus*, and other species, such as *R. alexandrinus*, *concolor*, etc. In a number of instances the disease has become endemic among other rodents, many of which are highly susceptible. In 1910–11 a great epidemic occurred in Manchuria following an epizoötic amongst marmots, *Marmota* (*Arctomys*) *bobac*, which is hunted for its skins. The disease is still very frequent among people who hunt these animals or handle their skins. In California, where plague first got a foothold among the rats of San Francisco's Chinatown in 1900, the disease eventually spread to the ground squirrels, *Otospermophilus grammurus beecheyi*, and over 20 years of effort have not yet eliminated it. In Central Asia and southeast Russia the disease has similarly become established in ground squirrels (susliks) of the genus *Citellus* (principally *C. mugosauricus* and *C. fulvus*), and a most determined and energetic fight is now on to bring the situation under control. In South Russia, contrary to experience in other countries, mice act as plague carriers. In Orange Free State in South Africa the gerbilles and karoo rats function in a similar manner; most of the veldt rodents are said to be even more susceptible to plague

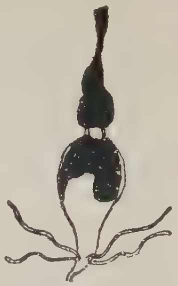

FIG. 228. Digestive tract of flea plugged with solid growth (in black) of plague bacilli. (After Manson.)

than black rats. In most other parts of the world the domestic rats are still the prime reservoirs of the disease, but the spread of plague into local wild rodents must constantly be kept in mind as a dangerous possibility.

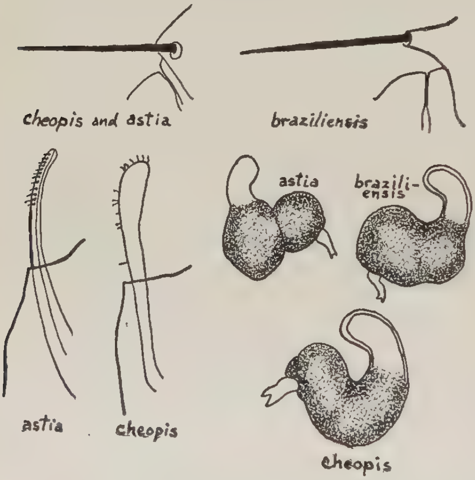

Fig. 229. Differential characters between common species of *Xenopsylla*. Above, antepygidial bristle; at left below, 9th sternites; at right below, spermathecæ. (From Tropical Diseases Bulletin.)

The relation of fleas to plague is even more involved, and depends on the species, abundance, habits, susceptibility to climatic conditions, effects of plague infection, and probably other undetermined factors. A very large number of fleas have been experimentally proved to become infected with plague, but this fact in itself means very little; the efficiency of fleas as transmitting agents of plague in nature is a far more complicated matter than the mere infectivity of the insects. This is perhaps nowhere better exemplified than in the case of *Xenopsylla cheopis* and *X. astia* in India and Ceylon. Both species are capable of transmitting plague under experimental conditions; both species are abundant on rats, though frequently only one is present; and both species readily bite man. Yet it has been clearly demonstrated by Cragg in India and by Hirst in Colombo that plague is common only in places where *X. cheopis* is locally abundant; in fact in every part of the world where plague epizoötics become permanently established among domestic rats this species predominates, and the seasonal prevalence of plague coincides with the seasonal prevalence of this flea. In the absence of this species only sporadic outbreaks of plague in cities need be feared. On the other hand, in localities where *X. cheopis* is uncommon and *X. astia* predominates, plague is either sporadic or entirely absent. Not enough is yet known about the relation of *X. braziliensis* to plague, but this species, too, seems to be an inefficient transmitter in nature. Experimentally the efficiency of *X. astia* as a plague transmitter is intimately connected with climatic conditions. Under the hot moist conditions of Colombo and Madras where *astia* predominates, this species is an inefficient transmitter, whereas it functions well under the cooler conditions of Bombay in the cool season. *X. cheopis*, on the other hand, thrives best in localities with cool seasons, but establishes itself locally in other places also, and is apparently a good plague transmitter under a wider range of climatic conditions. The principal reason for the inefficiency of *astia* as a plague transmitter, especially in such climates as that of Colombo and Madras where it is most likely to be prevalent, according to Hirst, probably lies in the fact that this flea, in contrast to *cheopis*, quickly succumbs to a heavy plague infection; a " blocked " flea of this species was never found alive at laboratory temperatures in Colombo even in cool weather. Since *astia* bites at shorter intervals than *cheopis*, blocking of the proventriculus leads to a more rapid death, by starvation or desiccation, under conditions of high temperature or low humidity, than is the case with *cheopis*.

The case against *Ceratophyllus fasciatus* is similar. The fact that plague fails to become permanently established in the northern cities of America and Europe, where *X. cheopis* is largely replaced by *C. fasciatus*, is significant. When plague is introduced into northern ports it is temporarily spread among rodents by the latter flea, and from man to man by *Pulex irritans*, but it soon dies out. Various species or *Xenopsylla* and *Ceratophyllus* are capable of extending epizoötics started by *X. cheopis*, or of extending their seasonal duration, but the outbreaks are usually if not always initiated by *cheopis*. In the case of endemic plague among wild rodents other fleas become involved in the transmission from rodent to rodent, but their rôle as transmitters to man is very limited; in many instances the human cases result from handling the diseased animals or their skins, or from direct acquisition of fleas from freshly killed animals or from their burrows, and not from the active pursuit of man by fleas liberated from dead rats in or about human habitations. Thus the disease is kept alive among Mongolian marmots by *Oropsylla* (*Ceratophyllus*) *silantiewi;* among ground squirrels of southeast Russia and Central Asia mainly by *C. tesquorum* and *Neopsylla setosa;* among the veldt rodents of South Africa probably by *Xenopsylla eridos*, *Dinopsyllus lypusus*, *Chiastopsylla rossi*, and others; among California ground squirrels by *Ceratophyllus montanus* (=*acutus*) and *Hoplopsyllus anomalus;* and among field rats in Java by *Stivalius ahalæ*. Many of these fleas remain in the burrows long after they have been deserted, eventually attacking new residents of the burrows or dying of starvation.

The dispersal of plague from one part of the world to another is usually accomplished by the transportation of infected rats on ships or railways, together with their fleas. Transportation of rats is not necessary. *Xenopsylla cheopis* is able to live and to reproduce apart from its host, as for instance in grain in which rats were formerly present.

This flea is more readily dispersed than most species for this reason, and live individuals may be landed with produce, even in the absence of rats, after several weeks at sea. In ports such as Colombo changes of climate unfavorable to the reproduction of *X. cheopis* may be neutralized by continuous importation of fresh fleas with grain.

Fleas and other Diseases. — Experimentally fleas are able to transmit tularemia (see p. 434) among rodents; the disease has been transmitted between California ground squirrels by *Ceratophyllus montanus* (= *acutus*). Whether or not fleas are important in disseminating the disease among rodents in nature is unknown.

Fleas have long been suspected of transmitting leishmaniasis (infantile and canine kala-azar) in the Mediterranean region. The frequent occurrence of the disease in both children and dogs first suggested fleas, since these are the principal insect parasites which are common to both hosts. Basile performed a number of experiments which indicated that the dog flea, *Ctenocephalus canis*, was the intermediate host and transmitting agent of the parasite. Later, however, much doubt was thrown on the validity of this work. Not only dog fleas but many other fleas as well harbor a *Herpetomonas* parasite in their intestines which is a specific flea parasite and has no relation to *Leishmania* infections in vertebrates (see p. 120); this form was, however, confused with the developmental stages of *Leishmania* by a number of earlier workers, including Basile. Later very carefully controlled experiments by da Silva, Wenyon, and Nicolle and Anderson have been uniformly negative with respect both to development of *L. donovoni* in fleas and also to the transmission of the disease to dogs by these insects. Fleas have also been tested both by Wenyon and Laveran as intermediate hosts and transmitting agents of *Leishmania tropica* of Oriental sore, but with entirely negative results. Nöller has described a method by which fleas can be tethered to a wire so that they can be individually studied during and after feeding. This has made it possible to eliminate fleas already infected with a *Herpetomonas* by examining feces ejected during feeding, and to keep subsequent individual records of fleas after feeding.

Fleas serve as natural intermediate hosts for the non-pathogenic rat trypanosome, *T. lewisi*, and quite likely for the related trypanosomes of other rodents also. *Trypanosoma cruzi*, however, although it develops in such different arthropods as ticks and bugs, undergoes rapid degeneration in fleas. In one instance surra, caused by *T. evansi*, has been reported as having been transmitted by the cat flea, *Ctenocephalus felis*, but there is no evidence of other trypanosomes of the larger mammals or man developing in fleas.

Fleas have been suggested as the possible transmitting agents of

Spirochæta crociduræ of shrews in Africa, a species which is believed to be identical with the parasite causing the strain of human relapsing fever which occurs at Dakar, in which case fleas may also transfer the infection from rodents to man. Spirochætes have been found in the guts of cat fleas in India by Patton.

Fleas serve as intermediate hosts for certain kinds of tapeworms. The common dog tapeworm, *Dipylidium caninum*, which occurs occasionally in man, utilizes the dog flea, *Ctenocephalus canis*, as an intermediate host. The eggs of the worm are devoured by the larvæ of the flea, and the six-hooked embryos remain in the larvæ in a state of rest, and only proceed with their development into cysticercoids after the flea has reached the adult stage. *Hymenolepis diminuta*, normally a parasite of rats but occasionally found in man, also utilizes fleas (*Ceratophyllus fasciatus* and *Xenopsylla cheopis*), as well as a variety of other insects, as intermediate hosts. Cysticercoids with scoleces resembling that of *Hymenolepis nana* have also been found in fleas, but they probably belong to other species of *Hymenolepis*.

Important Species

Human Flea. — The only species of flea which is known to be a parasite of man primarily, with the exception of the chigger, is the appropriately named human flea, *Pulex irritans*, though in many places man is annoyed more by certain other species which are primarily parasites of his domestic animals. The human flea is not exclusively a parasite of man. It also attacks badgers, skunks, dogs and other carnivores, occasionally occurs on rats and mice, especially in houses and ships, and has been taken on the blacktail deer, *Odocoileus columbianus*.[1] In some localities it is said to abound on pigs. It is now cosmopolitan in distribution, probably having originated in Europe, whence it was introduced with Europeans to all parts of the world. It is relatively rare in the tropics since it is killed by temperatures much over 85° F. This flea is the species which has made California as famous for its fleas as is New Jersey for its mosquitoes. The relatively cool humid summer climate combined with a mild wet winter make the Pacific Coast of the United States an ideal place for this pest. Though more or less of a nuisance throughout the year in mild climates, this flea is less troublesome in winter, due to relative inactivity, to slower reproduction, and to the fact that small mammals are more commonly attacked at this time of year.

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[1] Specimens of fleas taken in considerable numbers on deer in northern California by F. C. Clarke, of the California Fish and Game Commission, were identified by Prof. R. W. Doane of Stanford University as *Pulex irritans*. On account of the distinctive habits of these deer fleas, Clarke (in litt.) believes that they should be considered a variety of *P. irritans*, for which he proposes the name *P. irritans cervi*.

The human flea is readily distinguished from most common species in temperate climates by the absence of any combs, either on the head or thorax. From the Indian rat flea, *Xenopsylla cheopis* (Fig. 225), it is difficult to distinguish, the essential difference being the presence in the rat flea and absence in the human flea of a vertical chitinous thickening of the mesosternum, *i.e.*, the plate to which the middle leg is articulated on either side. The antennæ of the human flea are shorter and more knoblike than are those of *Xenopsylla*, and the male genitalia differ.

The human flea secretes itself in crevices and cracks of houses, in floors, rugs, bedding, etc., coming forth chiefly at night to pierce the flesh and suck the blood of its hosts. The susceptibility of different individuals to flea bites is variable. The irritation that is normally produced, probably chiefly as a result of the injection of the insect's salivary secretions into the wound, causes the formation of a reddish pimple with more or less swelling. Some people, however, are apparently entirely immune to flea bites and feel no pain from them. The writer is one of these fortunate individuals. On his first visit to California he had been fully warned concerning the ravages of the fleas but found to his pleasant surprise that the only discomfort felt from fleas was the tickling occasionally caused by their movements beneath his clothing. A college roommate, however, was attacked to such an extent as to be unable to sleep, and spent a considerable part of many nights in pursuit of the wily fleas and in violent massaging of painful wounds.

As has been noted, the human flea may act as a transmitter of plague, though it is not the chief villain in the spread of this disease.

Dog and Cat Fleas. — Next in frequence to the human flea as a parasite of man is the dog flea, *Ctenocephalus canis*, and the closely allied cat flea, *C. felis*. In the southeastern United States where the flea scourge is as great if not greater than in California, the dog flea is the species usually met with. During the moist hot summers this species becomes exceedingly abundant. Although primarily a parasite of dogs it willingly includes man in its bill of fare if opportunity offers, and also attacks cats, rats and other mammals. The usual fleas of cats, however, are now generally considered to be specifically distinct from the dog flea. The cat flea is the one of the two species more frequent in India, where it is a common parasite of dogs as well as cats. The cat flea has a longer and more slender head than its near relative. Both species can readily be distinguished from any other common species with similar habits by the presence of *two* conspicuous combs, one along the ventral margin of the head, the other on the pronotum (Fig. 226*A*).

The eggs of dog and cat fleas are usually laid loosely in the fur of their host, whence they readily fall out when the host shakes himself or is settling himself for a nap. They develop in the dust and dirt of kennels, woodsheds, house floors or other places where infested animals are likely to go. Houses, of course, become infested through the agency of infested animals, and since the fleas, once in houses, encounter man more readily than they do the original hosts, man is very likely to suffer from their attacks. Patton and Cragg found the inside of a hat, in which a kitten had slept overnight, so full of flea eggs that it looked as if it had had sugar sprinkled in it from a sifter. Another author collected a teaspoonful of eggs from the dress of a lady who had held a kitten in her lap for a short time. The writer has been able to find a similar quantity of eggs by dusting a smooth hardwood floor after an infested dog had indulged in one vigorous shake. With these instances in mind one can readily understand how houses into which infested pets are admitted become overrun with fleas.

The dog flea, from its habits, is the species most frequently implicated in the transmission of the dog tapeworm (*Dipylidium*) infection to children. Since this species will feed on rats it may occasionally act as a transmitter of bubonic plague, though its preference for dogs or cats would preclude a frequent occurrence of this.

Rodent Fleas. — The various species of fleas which infest rats, ground squirrels, and sometimes other rodents are only accidental parasites of man. Most of them readily attack him if opportunity offers, but are normally found only in the fur or habitats of the normal hosts. If it were not for their enormous importance in the spread of bubonic plague, they would need no special consideration.

Due to its intimate connection with bubonic plague the Oriental rat flea, *Xenopsylla cheopis* (Fig. 223) is of prime importance. The Xenopsyllas are rather short, stout fleas, resembling *Pulex* in having a single row of spines on each abdominal segment, no combs, and antennæ segmented only on the posterior side, but differing in the presence of a vertical as well as a horizontal thickening on the larger mesosternite. Though most of the members of the genus are confined to Africa and Asia, *X. cheopis* has now a world wide distribution, having accompanied its normal hosts, the domestic rats, to all warm seaports in both the Old and New World. Its original home was probably the Upper Nile Valley. It is essentially a flea of warm climates and does not establish itself permanently in countries with long freezing winters. In the United States it is the dominant species on rats in southern ports, but is relatively rare inland and in northern ports. It was probably originally a parasite of the black rat, just as *Ceratophyllus fasciatus* is of the brown rat, but in some ports in southern United States the brown rat has an almost pure infestation with *Xenopsylla cheopis.* De Raadt has observed that these fleas frequently drop out of their rat hosts, and if they do not readily find them again will willingly attack man. The fleas are easily dispersed by commerce both on their hosts and in such produce as grain which was formerly infested with rats.

There are a number of other species of *Xenopsylla* on rats, of which *X. astia* has already been discussed at some length. *Xenopsylla cheopis* and *X. astia* are readily distinguished by the form of the spermatheca in females (Fig. 229) and by the 9th abdominal sternite in the males. *X. astia* is an even more tropical species than *cheopis,* its original home probably being in the hot damp countries of southeast Asia. The distribution of these two species is very irregular, and is not correlated with the usual factors influencing insect distribution. Akyab, Burma, for instance, has an almost pure *astia* infestation on its rats, while Rangoon with a similar climate has about equal proportions of both species. *X. braziliensis* probably came originally from Central Africa, where in many places it is the prevalent rat flea, but it also occurs irregularly in hot parts of India, Brazil and other tropical countries. *X. eridos* is a species found on veldt rodents in South Africa, and is associated with endemic plague there.

In temperate climates the genus *Xenopsylla* is largely replaced by *Ceratophyllus* (Fig. 226*C*). This contains fleas with only the pronotal comb present, with two rows of bristles on each abdominal segment, and with an inconspicuous notch or tubercle on the front of the head. It contains a number of important species, most of which live on rodents. *C. fasciatus* is the prevalent rat flea of temperate climates. This species requires much cooler temperatures for its development, and the larvæ seem unable to develop without blood from the feces of the adults. As already noted, this flea can temporarily keep up plague epizoötics, and seasonally extend them, but it seems seldom if ever to initiate them. It readily attacks man in the absence of its natural host, but according to Strickland it seems to require rat blood before any eggs are laid. Several other species of *Ceratophyllus* and closely related genera are important as agents in keeping up plague infections in wild rodents. Such are *C. montanus* (=*acutus*), of California ground squirrels, *Oropsylla silantiewi* of Mongolian marmots, and *C. tesquorum* of ground squirrels in Asiatic Russia. *C. gallinæ* attacks birds; it is common on chickens in Europe, and has been introduced into America probably with English sparrows. Although it can transmit plague experimentally, it is of little or no importance in nature.

A few other rodent fleas deserve special mention. In China, Japan and some of the East Indian Ids. the prevalent rat flea, except where *X. cheopis* has been introduced, is *Stivalius* (formerly *Pygiopsylla*) *ahalæ.* This resembles a *Ceratophyllus* but lacks the notch on the front of the head. It requires more moisture than *X. cheopis* and, except at high altitudes, finds the nests of house rats too dry for breeding; in most parts of the Orient it is, therefore, primarily an out-door flea and its relation to plague transmission is uncertain. *Ctenopsylla segnis* (=*Leptosylla musculi*) Fig. 226*B*, primarily a mouse parasite, also occurs on rats in temperate countries, where it may be a minor factor in plague epizoötics, but it rarely bites man. It is easily recognized by its vertical genal comb of four spines and two spine-like bristles near the front of the head. *Neopsylla setosa*, suspected, along with *Ceratophyllus tesquorum*, of maintaining plague in Central Asian ground squirrels, has a genal comb of only two spines, which cross each other.

Chiggers. — The chigger, chigoe, jigger or sand flea, *Tunga penetrans* (Fig. 230), as it is variously called, is one of the most despised pests of tropical countries. It is common in many parts of tropical America and Africa and neighboring islands, and also occurs in India, though it does not thrive there as well. It is absent from China, but another species, *T. cæcigena* (=*lagrangei*) has been found on the ears of rats in Shanghai. It is a very small flea of the family Echidnophagidæ, about one mm. in length, with no comblike spines and relatively slender legs. It has a very conical pointed forehead, like a helmet worn with the point forward. The males and virgin females of this species are similar to other fleas in habits, except that they attack a wide range of hosts. Either man or pigs seem to be the principal hosts of this pest, but cats, dogs and rats are also attacked. It breeds especially in regions with sandy soil shaded by heavy underbrush, or in the earth floors of native houses. After emergence the fleas lie in waiting in débris on the ground and attack mainly the feet of animals or human beings which come their way. The particular importance of this flea lies in the fact that the impregnated females have the aggravating habit of burrowing into the skin especially in such tender spots as under the toe nails, where, nourished by the blood of the host, the eggs develop and cause the abdomen to swell into a great round ball as large as a pea, leaving the head and legs as inconspicuous appendages (Fig. 231). Only the two posterior

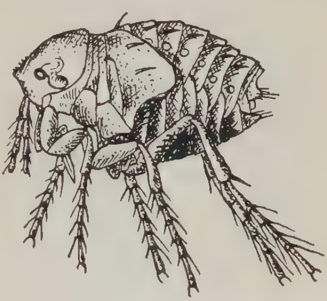


FIG. 230. Chigger or burrowing flea, *Tunga penetrans*, unimpregnated female. × 30. (After Karsten from Riley and Johannsen.)

segments of the abdomen do not enlarge; these act as a plug for the hole made in entering the skin. The eggs, up to a hundred in number, mature in about a week and are then expelled by the female through the protruding end of the abdomen. Sometimes the entire female is expelled with her eggs by the pressure of the inflamed tissue which surrounds her. The eggs, which fall to the ground, soon hatch into typical flea larvæ (Fig. 232). These, if they happen to fall on sandy soil under conditions suitable for their development, grow to maturity, pupate in a cocoon and emerge as adult insects in the course of ten days or two weeks.

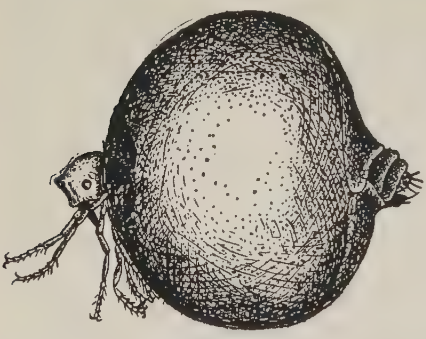


Fig. 231. Chigger or burrowing flea, *Tunga penetrans*, gravid female. × 18. (After Moniez.)

The wounds made by the burrowing female in the skin become much inflamed and very painful. Frequently the distended abdomen of a flea is crushed and the eggs released in the wound. In such cases the inflammation is greatly increased unless the crushed body and eggs are immediately expelled. As soon as the eggs are laid, or even before, the skin surrounding the wound ulcerates and pus is formed. The empty female flea is expelled. The sore which is left is very liable to infection by bacteria and frequently results in the loss of toes or even whole limbs through blood-poisoning. Quiros has pointed out that in Central America, where chigger infection is very common, especially in boys who play barefooted in the streets along which infected hogs are driven to public market, deaths from tetanus and gas gangrene from chigger wounds are very common. In Dutch Guiana chiggers have been suggested as a cause of elephantiasis of the foot in regions where *Wuchereria bancrofti* is absent; elephantiasis in filarial infections is always preceded by an inflammation of the lymph glands as a result of bacterial infection, and such inflammation is also caused by infection of chigger wounds. Chigger wounds have also been suspected as a cause of ainhum, a peculiar condition in which certain toes constrict and drop off, but Acton has demonstrated a totally different cause.

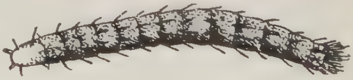


Fig. 232. Larva of chigger, *Tunga penetrans*. (After Newstead.)

Although usually only a few chiggers are present at a time, there are cases where hundreds infest a person at once, literally honeycombing the skin and making the feet or other parts of the body so sore that the victim is rendered a complete invalid.

The treatment of chigger wounds formerly consisted in the destruction of the fleas while imbedded in the wounds. This was done by applying various insecticides or pricking with a needle, the dead insect being removed after ulceration. A much better method is to enlarge the entrance hole of the flea with a clean needle and remove the parasite entire. The wound should then be carefully dressed and protected until healed. An ointment recommended by Quiros consists of 2½ grams salicylic acid and 10 grams ichthyol in 10 grams of yellow vaseline. Bathing of infected parts with kerosene oil is also recommended.

Chiggers can be avoided to a large extent by the use of high boots, or shoes and leggings. Walking barefooted in chigger-infested regions is almost sure to result in attacks by these pests. Houses, yards, etc., in chigger regions should be kept carefully clean of dust, dirt and débris which might favor the development of the parasites. In Central America Quiros recommends, as one of the best preventive measures, a prohibition against driving hogs affected with chiggers through the streets, along with regulations for treating affected hogs where they are raised. According to Penschke, in German East Africa, attacks by chiggers can be prevented by thoroughly rubbing the feet every two or three days with vaseline to which has been added a few drops of lysol or cresol soap (15 drops to 3½ oz. of vaseline).

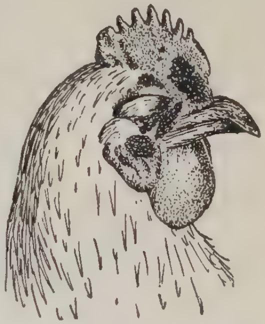


FIG. 233. Head of chicken infested with chicken flea, *Echidnophaga gallinacea*. (After Bishopp.)

Sticktight Flea. — The "sticktight" flea, *Echidnophaga gallinacea* (Fig. 233), is another member of the family Echidnophagidæ which may be a human pest. It is a small dark-colored flea which very commonly attacks chickens in nearly all tropical and subtropical countries, including the southern United States. Although the normal host is the chicken, other poultry, dogs, cats, domestic rabbits, rats and other animals, as well as man, are attacked. This species gets its name from the tenacity with which it adheres to its host. It is gregarious, collecting in dense masses on the heads of poultry (Fig. 233), in the ears of mammals and in other places. It burrows to some extent and probably deposits its eggs in the exudate which nearly covers the flea. It is not averse to attacking man, especially children, but since it is not so active as other fleas it can easily be found and removed. No disease is known to be transmitted by this flea.

Prevention. — Strict cleanliness in private homes or public buildings prevents fleas from breeding in them. Uncared-for carpets and straw mattings afford excellent breeding grounds for the human flea, as do dusty cracks between floor boards, unswept corners under sinks, and any other place where the eggs and young, undisturbed, may obtain enough moisture to keep them from drying up. The use of bare hardwood floors with rugs which can readily be taken up and swept, and thorough sweeping in corners and under pieces of furniture, sinks, etc., do not give fleas an opportunity to breed in the home or in public buildings, and are therefore valuable preventive measures.

One of the best means of ridding an infested house of fleas is to sprinkle the floors with naphthaline and close the rooms for a day or two. This will effectually kill all adult and larval fleas, and the eggs may then be destroyed by washing the floors with hot soap-suds, a five per cent formalin solution, or one-tenth per cent solution of corrosive sublimate. It is claimed that alum swept into carpets or a solution of alum soaked into carpet paper prevents fleas from breeding.

Fleas are very susceptible to fumigation with hydrocyanic acid gas. Experiments by the U. S. Public Health Service show that fleas succumb to the amount of gas generated by two and one-half ounces of potassium cyanide in 1000 cubic feet of space. Fumigation with sulphur is also effective. Details of methods of fumigation with these substances will be found on p. 456. Sodium fluoride in the form of a crystalline powder scattered on floors or blown about by means of a dust-gun will probably prove effective against fleas, as it has against cockroaches and other insects. It is inexpensive and not dangerous to handle.

Various traps for the capture of adult fleas have been devised, one of the simplest and most effective being to clothe the legs in sticky fly paper, and wander about in the infested rooms. A badly infested building in Cornell University was cleared of fleas in this manner. A similar method has been used to get rid of chiggers in a military encampment in East Africa where other hosts were absent. The men went about barefooted and had the chiggers they collected removed each evening, as a result of which they soon became rare in that immediate vicinity. Another device, used by the Chinese, is a rod of bamboo, smeared with bird lime, fitted inside of a larger piece of bamboo which has holes cut in it. A trap of similar type may be constructed by fitting a piece of broomstick wrapped with sticky fly paper inside a wire cylinder (Fig. 234). Such a " flea stick " can be rolled about on floors or in beds and will collect a large proportion of the flea population. Another trap consists of a glass of water with about an inch of oil on the top of it fitted with a little wick in the center of a floating piece of cork. This is placed in the center of a dish of strong soapsuds and lighted at night. The light attracts the fleas, which leap headlong into the soapsuds. Sometimes guinea pigs are used for collecting rat fleas from infested dwellings, or for estimating the number of free rat fleas.

The destruction of fleas, especially cat and dog fleas, on domestic animals is often necessary in order to do away with a flea scourge. Dogs and cats, or other hosts, may be cleared of fleas by washing them in two or three per cent solution of creolin (about one tablespoonful to a quart of warm water), or some other derivative of creosote, or a similar solution of potassium sulphide. According to Bishopp, the solution should be worked into the hair with a brush, and care should be taken to wet the fleas which crowd toward the head of the animal. After about ten minutes the solution should be washed off with warm water and soap, at least in delicate-skinned animals such as cats, to avoid a burning effect. Another method of treatment is to rub powdered naphthaline into the fur. This causes the fleas to emerge from the fur in a stupefied condition in which they are easily captured and destroyed. Except to sicken cats slightly for a day or two this treatment has no ill effect on the host.

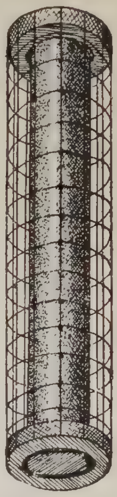


FIG. 234. A modification of the Chinese flea trap. Constructed of a broomstick wrapped with sticky fly paper, fitted in a cylinder of wide-meshed wire net. (After Bishopp.)

Of temporary value in flea-infested places is the use of repellents, such as oil of pennyroyal, eucalyptus oil, etc., smeared on shoes or clothing, or between bed sheets. Beds may be isolated by elevating them to some distance from the floor, or by surrounding them with a band of sticky fly paper 12 to 14 inches wide. Where perfect protection from fleas is desired, as in a plague-smitten city, all of these protective measures, as well as fly-paper wrapped legs, and any other means which may come to mind should be made use of. These should be followed up by the more permanent measures leading to the extermination of both larval and adult fleas.

Rat fleas, of course, can only be controlled by control of the hosts. The methods of fumigation which destroy rats also destroy fleas. In houses or ships where plague has occurred, thorough fumigation is the only effective method of eliminating fleas.

CHAPTER XXVI

BLOOD-SUCKING FLIES

Importance. — From a medical point of view the Diptera are far more important than all other arthropods put together, for in this order are included the normal transmitters of malaria, trypanosomiasis, yellow fever, dengue, papataci fever, various types of filariasis, and in all probability kala-azar and Oriental sore, and verruga or Oroya fever. Without their transmitters these diseases would probably entirely disappear. Other blood diseases, such as anthrax, are mechanically conveyed by flies, and the housefly and other non-biting flies are involved in the mechanical transmission of all kinds of filth diseases. One such fly, *Hippelates pusio*, has been found to be an important transmitter of "pink-eye." Besides all this, the Diptera include also all the insects which infect wounds, skin, nasal passages or digestive tract as maggots.

General Structure of Diptera. — To understand the relations of these numerous important insects and their classification, we must make a brief survey of the characteristics and classification of the order Diptera. The whole order can usually be distinguished readily from other insects by the fact that there is only one pair of membranous wings, the second pair of wings being represented only by an insignificant pair of knobbed rodlike appendages known as halteres (see Fig. 170, *h.*). Even in those forms in which the wings are secondarily absent the halteres are usually present. In many of the Cyclorrhapha there are membranous expansions at the base of the wings posteriorly which are folded under the wings when at rest. These are called alulæ or calypteres, and are sometimes quite conspicuous, as in the houseflies and their allies. The so-called muscoid flies, which constitute the main division of the Cyclorrhapha, are divided into two subsections, the Acalyptratæ and Calyptratæ. The calypteres are well shown in Figs. 237 and 248. The legs consist of the usual segments (see p. 386), with usually long coxæ. The tarsi are usually terminated by two claws with pad-like "pulvilli" under them, and often a third appendage, the "empodium," between them, either bristle-like or resembling a third pulvillus. The head is joined to the thorax by a very slender, flexible neck. The thorax itself consists of one mass on account of the fusion of its three component parts, and the abdomen usually consists of from four to nine visible segments and is terminated by the ovipositors or egg-laying organs in the female, and by the copulatory organs in the male. The head is provided with a pair of antennæ, a pair of maxillary palpi and a proboscis composed of or containing the mouthparts. The antennæ and also the palpi are of considerable use in classification; the extent of the variations in the antennæ may be gathered from Fig. 235. In the more generalized families, *e.g.*, the Nemocera, the antennæ consist of many segments which, except the basal two, are similar in form (Fig. 235 *A* and *B*), and often bear whorls of hairs which in the males often give a plumose effect, *e.g.*, in male mosquitoes. In more specialized families the terminal segments tend to coalesce more or less (Fig. 235*C*) as in the tabanids and other Brachycera, or the segments beyond the third are reduced to a simple or plumose bristle or arista which appears as an appendage of the enlarged third segment (Fig. 235 *D* and *E*), as in nearly all of the Cyclorrhapha (fleshflies, houseflies, tsetse flies, etc.). The mouthparts are profoundly modified in accordance with the habits of the flies. In the botflies, in which the adults live only long enough to reproduce their kind, the mouthparts and even the mouth are much degenerated; in the non-blood-sucking forms, such as the common housefly, the mouthparts are more or less fused into a fleshy proboscis which is used for lapping up dissolved foods; in the blood-suckers, which are the forms that particularly interest us here, the mouthparts are developed into an efficient sucking and piercing apparatus. In some, *e.g.*, mosquitoes (Fig. 276) sandflies, blackflies and horseflies (Fig. 254), the lower lip acts as a sheath for the other parts which are fitted for piercing and sucking; in others, *e.g.*, the stable-fly, *Stomoxys* (Fig. 270), and the tsetse flies, *Glossina* (Fig. 259), the lower lip itself forms a piercing organ, and the epipharynx and hypopharynx form a sucking tube, the mandibles and maxillæ being absent.

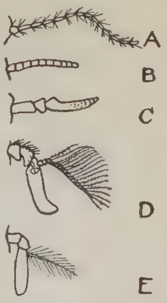


Fig. 235. Types of antennæ of Diptera; *A*, mosquito, female; *B*, blackfly; *C*, gadfly (tabanid); *D*, tsetse fly; *E*, stable-fly.

Life Histories. — All of the Diptera have a complete metamorphosis (see p. 391), and sometimes undergo a most profound remodeling of the entire body during the usually short pupal stage. The life history, beyond the fact that a complete metamorphosis occurs, varies within very wide limits. Most flies lay eggs, but some, *e.g.*, the screw-worm fly, *Cochliomyia* (or *Chrysomyia*), and allied species, produce newly hatched larvæ or eggs which are just at the point of hatching, while still others, *e.g.*, the tsetse flies, *Glossina*, do not deposit their offspring until it has undergone its whole larval development and is ready to pupate.

The larvæ of Diptera may be simple maggots with minute heads and no appendages and capable of only limited squirming movements, *e.g.*, the screw-worms (Fig. 304), or they may be quite highly developed, active creatures, *e.g.*, the larvæ of mosquitoes, midges, etc. Many are aquatic, many others terrestrial; usually the eggs are laid in situations where the larvæ will find conditions suitable for their development, and the flies often show such highly developed instincts in this respect that it is hard not to credit them with actual forethought. The pupæ of the Diptera also vary widely. In one great suborder, Orthorrhapha, the pupa is protected only by its own hardened cuticle, or, as in the blackflies, a spun cocoon, and is often capable of considerable activity; from this "obtected" type of pupa (Fig. 236*B*) the adult insect emerges through a longitudinal slit along the back. In the other suborder, Cyclorrhapha, the pupa retains the hardened skin of the larva as a cocoon-like covering or "puparium," and is usually capable of very slight movement; from this "co-arctate" type of pupa (Fig. 236*A*) the adult escapes by pushing off the anterior end of the puparium; except in a few families (Series Aschiza) this is done by means of a hernia-like outgrowth on the front of the head. This outgrowth, called the "ptilinium" (Fig. 237*A*) shrinks after the fly has emerged, but leaves a permanent crescent-shaped mark on the head known as the "frontal lunule" (Fig. 237*B*) which embraces the bases of the antennæ, and gives a dependable clue to the early life of the insect. Adult flies are usually not long lived, and often live only a few days, just long enough to copulate and lay their eggs. Some species, however, *e.g.*, mosquitoes, may live for several months.

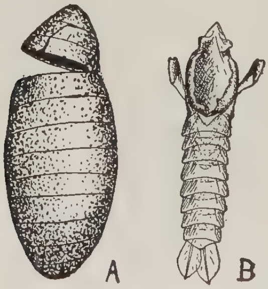


Fig. 236. Types of pupal cases, showing manner of emergence of adults. *A*, empty case of blowfly, typical co-arctate pupa of Cyclorrhapha; *B*, empty case of mosquito, typical obtected pupa of Orthorrhapha.

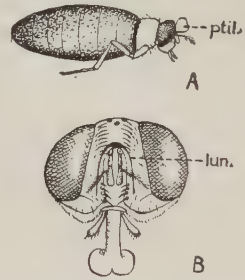


Fig. 237. *A*, fly emerging from pupal case, showing bladder-like ptilinium (*ptil.*) by means of which the end of the case is pushed off; *B*, face of fly showing scar or lunule (*lun.*) left by drying up of ptilinium. (After Alcock.)

The order Diptera, as already indicated, is divided into two great suborders, the Orthorrhapha and the Cyclorrhapha. The Orthorrapha are further divided into two sections, the Nemocera, with elongate antennæ consisting of a series, beyond the first two, of similar segments, and the Brachycera, with short antennæ in which there is a more or less well-developed tendency to a fusion of the segments beyond the third. Of the Orthorrhaphous Diptera considered here, the mosquitoes, sandflies, midges and blackflies belong to the Nemocera, and the tabanids to the Brachycera. The Cyclorrhapha are further subdivided into divisions above families as follows:

Suborder Cyclorrhapha
- *Series I. Aschiza.* Without ptilinium or frontal lunule. Includes no species of parasitological interest.
- *Series II. Schizophora.* With ptilinium and frontal lunule.
  - *Section I. Myodaria.* Forms with opposite legs of each pair close together; abdomen distinctly segmented; larval development, except in tsetse flies, not in uterus of mother. Muscoid flies.
    - *Subsection I. Acalyptratæ.* With alulæ or calypteres rudimentary or absent. Very small, non-blood-sucking flies. Includes the cheeseflies.
    - *Subsection II. Calyptratæ.* With well-developed alulæ or calypteres. Includes houseflies, stable flies, tsetse flies, fleshflies, botflies, etc.
  - *Section II. Pupipara.* Opposite legs of each pair widely separated; segmentation of abdomen obscure; larval development completed in uterus of mother. All parasites, sucking blood from birds or mammals, but none parasitic on man. Includes "sheep tick," louse flies, bat flies, etc.

Of the forms with which we shall deal, all except the cheesefly, mentioned in the chapter on "Myiasis," belong to the Calyptratæ. In the present chapter there will be considered all of the important blood-sucking Diptera except the mosquitoes which, on account of their outstanding importance, are made the subject of a separate chapter. The Diptera which are parasitic as maggots will also be considered in a separate chapter on "Myiasis."

Phlebotomus or Sandflies

General Description. — Phlebotomus flies, commonly known as "sandflies" are minute mothlike midges which are found in nearly all warm and tropical climates of the world, with the exception of Australia and the East Indian Islands. In Australia (Queensland) they are represented by an allied fly of the same family, *Pericoma townsvillensis*, which is said to be a very severe biter, producing swellings which may last three weeks. They belong to the family Psychodidæ, which includes a large number of species of flies found all over the world, nearly all of which resemble tiny moths on account of their very hairy bodies and mothlike pose. The latter characteristic, however, is not shared by the genus *Phlebotomus*. The latter is the only genus, except *Pericoma*, containing habitual blood-suckers with a long proboscis; in all other members of the family the proboscis is short and inconspicuous. The members of the family Psychodidæ are easily recognized by the characteristic wing venation, with nine longitudinal veins reaching the edge of the wing, and with no cross-veins except near the base. The characteristic venation in *Phlebotomus* is shown in Fig. 238.

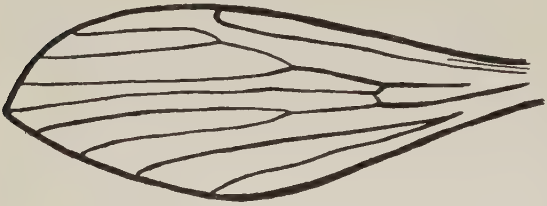


Fig. 238. Wing venation of *Phlebotomus argentipes*. (After Sinton.)

The sandflies (Fig. 240*D*) are small dull-colored insects, usually yellowish or buff, slender in build, with hairy body and very long and lanky legs. The hairy-veined wings are narrow, somewhat the shape of mosquito wings, and are held erect over the body when the insect is in repose. The antennæ are long, consisting of a series of beadlike segments with whorls of hairs at the joints. The proboscis is longer than the head, and consists of a fleshy labium, the distal third of which consists of a pair of movable "labella," which can be spread apart when the insect is piercing. There are five piercing organs: a pair of dagger-like mandibles with saw-like teeth near the tip, a pair of flat, blade-like maxillæ, also toothed, and a blade-like hypopharynx through the solid chitin of which runs the salivary duct, opening some distance from the tip and being continued as a groove. The labrum is dagger-like, but is provided with sensory hairs and spines and is probably not used as a piercing organ. The piercing organs project beyond the tip of the labium when at rest and the labium does not bow back when the other parts are in action as is the case with mosquitoes. The male genitalia consist of three appendages (Fig. 239), the details of which are of great value in identification. Sandflies vary from about 1.5 to 3.5

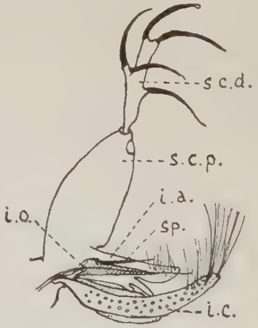


Fig. 239. Male genitalia of *Phlebotomus argentipes; s. c. d.*, superior clasper, distal segment; *s. c. p.*, superior clasper, proximal segment; *i. a.*, intermediate appendage, with spine (*sp*); *i. o.*, intromittent organ; *i. c.*, inferior clasper. (After Sinton.)

mm. in length, and so can easily crawl through the meshes of an ordinary mosquito net. Their bites are very annoying and in some species cause an amount of irritation which seems quite out of proportion to the size of the insect. The females feed exclusively on blood, often feeding only once and dying after the subsequent oviposition, but most species at least sometimes feed twice or oftener, laying eggs after each feeding. The preferred hosts vary with the different species; *P. minutus* seems to feed practically entirely on cold-blooded animals, particularly geckos; *P. argentipes* feeds by preference on cattle and then on man; *P. papatasi*, *sergenti* and *perniciosus* seem to take particular delight in human blood. The males of at least some species appear not to feed at all, subsisting on the remnants of the last larval food. One African species, however, is said to have biting males. Sandflies are very short lived, and even the females commonly die after the first oviposition, on the 5th or 6th day, and seldom survive more than a fortnight. They are nocturnal and seldom bite except in hours of darkness, and in some places they seem to forage for only an hour or so after sundown. During the day they hide in dark corners, cellars, crevices of rocks, etc. Their powers of flight are very limited. When disturbed on walls they usually fly only a few inches, appearing to hop rather than fly. In some instances *P. argentipes* has been found to be limited to certain rooms in which they breed, and are rarely found in adjoining rooms. Their breeding places are nearly always within 100 to 200 feet of their feeding places.

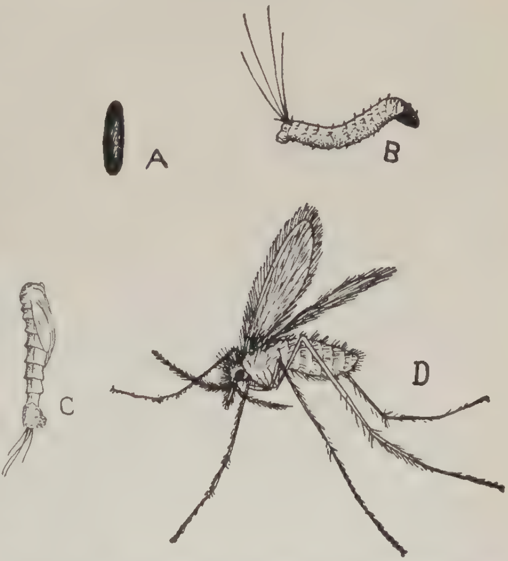


FIG. 240. Life history of sandfly, *Phlebotomus papatasi;* *A*, egg; *B*, larva; *C*, pupa; *D*, adult. *A*, × 80; *B*, *C* and *D*, × 8. (After Newstead.)

Life History. (Fig. 240.) — Most species of *Phlebotomus* lay their eggs in crevices of rocks, in damp cracks in shaded soil, on moist rubbish, in crannies or chinks in cement of dark cellars, between boards in privies and cesspools, and in other similar situations. Some species seem to show a decided preference for crevices in rocks, and find ideal situations in ruins of old stone buildings, crumbling rock fences, etc. In Malta Captain Marett found these insects breeding *only* in such places. In Peru, according to Townsend, the universal type of fence, a structure of rubble and loose rock, provides ideal breeding places for the species found there, whereas in Italy and Sicily the earthquake ruins furnish equally ideal breeding places for them (Fig. 241). The sandflies which occur in certain parts of Egypt are believed to breed in damp cracks in the sandy soil, since there seem to be no other suitable places. In India *P. argentipes* breeds in broken places in paved floors, in moist soil contaminated by the feces of fowls or goats, in damp crevices of mud walls plastered with cow dung, etc.

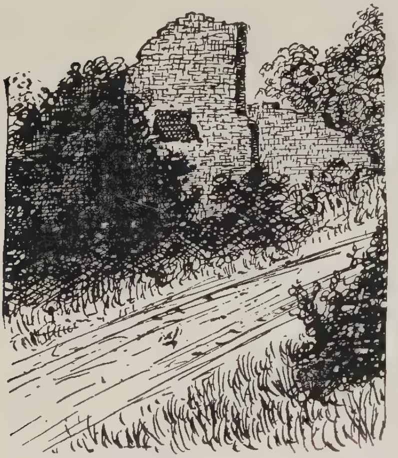


FIG. 241. An earthquake ruin in Sicily, affording favorite breeding places for sandflies.

The eggs are usually deposited within a few days after emergence and the first blood meal, and vary from 40 to 60 in number; some individuals lay second batches of similar size after a subsequent feed. When deposited the eggs are literally shot out by the female to a distance several times the length of the abdomen. The eggs are viscid and adhere to the surfaces with which they come in contact; it would seem that the peculiar method of ejecting the eggs is a protective adaptation, facilitating their deposition in the farthest reach of a crevice where even the tiny insect itself could not penetrate. The eggs are elongate and are of a dark, shiny brown color, with fine surface markings which vary in different species (Fig. 242).

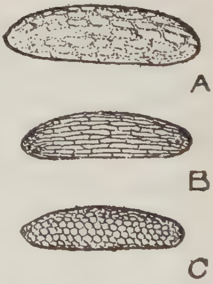


FIG. 242. Eggs of sandflies; *A, P. papatasi* *B, P. argentipes; C, P. minutus.* × about 200. (After Howlett.)

The incubation in the case of the common Old World *P. papatasi* requires from six to nine days under favorable conditions, but the eggs are very susceptible to external conditions, and die quickly if exposed to sunlight or if not kept damp. *P. argentipes* eggs may hatch in 4 days. The larvæ (Fig. 240*B*) are tiny caterpillar-like creatures with a relatively large head with heavy jaws (Fig. 243), and with two pairs of bristles on the last segment of the abdomen, one pair of which are sometimes nearly as long as the body and are held erect and spread out fanlike; in the newly hatched larvæ there is only one pair of bristles. The body is provided with numerous toothed spines which give it a rough appearance. These spines have been shown by Howlett to differ in different species and, together with the relative length of the caudal bristles, to form good identification marks. The whole length of the larva of *P. papatasi* when full grown is less than one-fifth of an inch, and is therefore not so large as an ordinary rice grain. It is quite active in spite of the fact that it has neither legs nor eyes; it progresses in the manner of a caterpillar, holding to a rock or board with the tip of the abdomen while stretching the body, then holding with the doubled-under head while drawing up the body again. It feeds on decaying vegetable matter, and probably also on moulds, etc. When exposed to light the larva of *P. papatasi* has the peculiar habit of flicking itself off the surface on which it has been resting. On approach of danger, *Phlebotomus* larvæ often "play 'possum" and feign death. The larvæ of *P. argentipes* feed on dead parent insects, particles of feces of fowls, rabbits, rats, etc., and on other organic débris. In all species a high degree of humidity is required, and in the case of *P. argentipes* the wet-bulb temperature must not exceed 80° F. According to Roubaud these insects are "heterodynamic," *i.e.*, they do not all develop in the same manner, as is the case with many Muscidæ. But instead of having periods of suspended animation cyclically returning in all the individuals of certain generations, in sandflies, of some species at least, some individuals of each generation show this peculiarity, and remain in the larval state for considerable periods. Hibernation is probably always in the larval state.

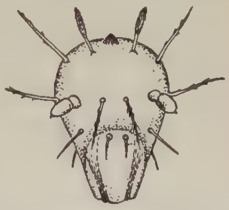


FIG. 243. Front view of head of *Phlebotomus minutus* larva. Much enlarged. (After Howlett.)

The full development of the larvæ requires from two weeks to two months or more, depending almost entirely on the temperature. Larvæ which hatch at the beginning of cold weather do not pupate until the following spring. When, after several moults, they go into the resting pupal stage the last larval skin with its caudal bristles remains adhering to the posterior end. The pupa (Fig. 240*C*) is characterized by a very rough cuticle over the thorax, but can be identified best by the adhering larval skin. It is colored so much like its surroundings, and looks so much like a tiny bit of amorphous matter, that it is very difficult to find. The pupæ are less susceptible to drying than are the larvæ. In warm weather the adult insect emerges after from six to ten days, but this is much prolonged by low temperatures. The entire life cycle from the laying of the eggs to the emergence of the adults may be passed through in a month in hot weather, though it takes two months or more in cool weather. In Malta, according to Newstead, the cycle takes about three months.

Sandflies and Disease. — In recent years sandflies have come into the limelight as disease transmitters. They have been known to transmit three-day fever, now usually known as papataci or sandfly fever, since 1908, when Doerr experimentally proved a suspicion that had long existed. Within more recent years sandflies have been found to be implicated in the more serious *Leishmania* diseases, both Oriental sore and kala-azar. There is also epidemiological and experimental evidence to show that a sandfly is the natural transmitter of verruga peruviana or Oroya fever.

Sandfly Fever. — This relatively mild febrile disease, which in many respects resembles dengue, is described on p. 197. It was experimentally shown by Doerr, in 1908, to be transmitted by *Phlebotomus papatasi*. The insects become infective about 6 or 7 days after feeding on a patient in the first or second day of the fever. Since sandflies are so short lived, and frequently suck blood only once, whereas the disease can be transmitted by apparently unfed flies, it has long been suspected that the infection was transmitted to the offspring; Whittingham (1922) proved this to be true by producing sandfly fever by the bites of flies bred from infected parents in England. There is no evidence as yet that any species but *P. papatasi* is able to transmit sandfly fever, and this species has been found in all places where the disease occurs except at Aden. Since the infection is of very short duration in man, it presumably is conserved from one season to another in the sandflies.

P. papatasi (Fig. 240*D*) is of medium size, reaching about 2.5 mm. in length, pale yellowish gray in color with a dull red-brown stripe down the middle of the thorax and a spot of the same color at either side. It is found in many parts of southern Europe, North Africa and in southern Asia. It has the typical habits of the genus, preferring to lay its eggs in crevices in damp cellars, in caves, cracks in broken walls, etc. In Malta the life cycle of this species has been observed to take about three months, but under warmer conditions, as in northwest India, the entire cycle requires about 40 days. The adults feed within 36 hours of emergence, and lay eggs in 4 to 5 days; a second batch of eggs may be laid after another blood meal. The eggs hatch in about 12 days, the larval stage lasts 21 to 25 days, and the pupal stage 7. According to Roubaud, not all the larvæ proceed with their development, however, some of them remaining in the fourth larval stage for a long time, and hibernating thus in cold weather.

The adult fly, as observed in Malta, chooses caves, cellars, catacombs and other similar places as its favorite hiding places. In northwest India they have been observed to hide in large numbers in cracks in the soil, in which they undoubtedly breed, protected from excessive heat or dryness. Sandbags used for raising the sides of tents may supply ideal hiding places. On still, warm nights they emerge to feed on human beings who are close at hand, but they avoid even light breezes, and can be kept away by the use of ceiling fans. Some houses are found to be much more infested than others, possibly due to the proximity of suitable breeding places and to the lack of breezes. Newstead found that dark rooms on the sheltered side of the first floor of a house were most likely to be infested; only one individual was found on the second floor. The distance which the adults travel is very short, but they may be carried by public conveyances, and infection has been known to be transplanted long distances by flies carried on coasting vessels.

Sandflies and Leishmaniasis. — There is probably no more baffling problem in connection with disease transmission than that of the natural transmission of the *Leishmania* infections, — Oriental sore, espundia and kala-azar. In recent years attention has been focused on sandflies, for certain species of these insects have been found to serve excellently as intermediate hosts of the *Leishmania* parasites. The steps in the development of this knowledge is more fully discussed in Chapter VII, pp. 126 and 133. A high percentage of certain species of sandflies fed on the blood or lesions of patients, or on cultures, become infected. The flagellates multiply and often become extremely numerous, and in particular species, which are in consequence considered the natural insect hosts, the development proceeds to the production of forms attached to the epithelium of the fore part of the stomach, and free flagellates invade the pharynx and buccal cavity. It is difficult to believe that the development of the *Leishmania* parasites could go as far as it does, and as regularly, in sandflies if these insects were not the natural hosts, or that development would occur even more readily in any other insects. If sandflies cannot transmit the infection by their bites, it is doubtful if any insect can. It has even been proved by Adler and Theobald that the flagellates are inoculated into blood while the flies are feeding through a rabbit skin membrane. When crushed flies infected with *Leishmania tropica* are inoculated into the skin they produce Oriental sores, from which the flies can again be infected, and when crushed flies infected with *L. donovani* are inoculated into the peritoneum of susceptible laboratory animals they produce systemic infections similar to the inoculation of spleen juice from a kala-azar case. Even more striking is the fact that the epidemiology of the diseases fits in so accurately with the sandfly transmission hypothesis that little room for doubt as to the rôle of sandflies is left. And yet, in spite of persistent and pains-taking experimental work in many parts of the world, neither Oriental sore nor kala-azar has yet been induced in man or animals by the bites of the flies, although exposed to more infective bites than could conceivably ever occur in nature. Only a hardened skeptic would at present absolve sandflies of complicity in the transmission of leishmaniasis, but how the trick is accomplished in nature is still an unsolved puzzle. The natural resistance of normal human beings or animals may be a factor.

The sandflies which have been incriminated in the case of Oriental sore are *Phlebotomus papatasi* and *P. sergenti*, which are widely distributed from the Mediterranean shores of Europe to India, over, indeed, a considerably wider range than Oriental sore. Sinton has suggested that perhaps *P. sergenti* is the main transmitter in India, since its distribution coincides with that of the disease, whereas the distribution of *P. papatasi* does not. The females of these two species are almost indistinguishable, but the North African workers have failed to find any males of *P. sergenti* in places where Oriental sore is very common, and so conclude that the species they have worked with is really *P. papatasi*. On the other hand, Adler and Theodor have found *P. sergenti* to serve as well, if not better, than *P. papatasi* as an intermediate host in Palestine. The solution of this problem remains to be worked out.

Whether or not the American form of dermal leishmaniasis, the cause of which is usually referred to as *Leishmania braziliense*, also develops in sandflies as intermediate hosts is not so certain. Specimens of *Phlebotomus intermedius* fed on espundia sores were found to develop herpetomonad infections and in one instance a *Leishmania* sore was produced on the nose of a dog by crushing a specimen of *Phlebotomus intermedius* on it. Some of the epidemiological data also suggest sandfly transmitters.

The species incriminated in connection with kala-azar in India is *Phlebotomus argentipes*, the distribution of which coincides excellently with that of the disease. This is a medium-sized sandfly, about 2.5 mm. long, grayish in color, with the sides of the thorax much lighter, and with the tarsi appearing silvery white. The adults seem to feed by preference on cattle, but attack man when cattle are not readily available; examination of the blood of fed flies by the precipitin test have conclusively proved this. "Wild" flies have never been found to feed on bird or reptile blood. The fly is very local in distribution, being found especially in masonry or thick mud-walled houses, and rarely in thin-walled bamboo-and-plaster huts. It is also abundant in damp, dark cow sheds and chicken houses. The male probably does not feed at all, whereas the female is a pure blood feeder; it appears always to feed in the dark. It breeds in earthen floors, and in damp sheltered earth which is contaminated by the droppings of chickens, cattle, goats, rats, etc. Under ideal conditions the life cycle requires about 30 days, — 4 for the eggs, 14 for the larvæ, and 7 for the pupæ. The adults live only three days without food, and usually die after the first oviposition when about 50 to 60 eggs are laid. The larvæ require a high degree of humidity, and can survive temperatures over 90° in a saturated atmosphere. They feed on their dead parents, dried blood, feces, etc. The adults fly only a few yards, and never rise to the second floor of a building.

Napier and Smith have shown that *P. papatasi* may occasionally serve as an intermediate host for *Leishmania donovani*, but of 101 females of this species fed on kala-azar cases only two got light infections, whereas of 102 *P. argentipes* fed on the same cases, 43 became infected, many of them heavily.

In China *P. major* var. *chinensis* becomes infected readily after feeding on infected hamsters (*Cricetulus griseus*), while a much smaller percentage of another common species, *P. sergenti*, does so. The distribution of *P. major*, however, does not coincide very perfectly with the distribution of kala-azar, and this species re-feeds with reluctance, whereas *P. sergenti* does so readily. *P. major* seems to have but one brood a year, while *P. sergenti* appears to have two. *P. minutus* in India and Africa, and *P. perturbans* in India and China, feed primarily on cold-blooded animals, especially geckos, and rarely bite man; apparently *minutus* never does. These species cannot, therefore be involved in the transmission of kala-azar; for a time it was suspected that geckos in North Africa might serve as a reservoir for Oriental sore, since herpetomonad flagellates can be cultivated from the blood of a percentage of them, and *P. minutus* was found to feed on them in abundance. Similarly in China, *P. perturbans*, which feeds readily on toads, is often heavily infected with crithidiform flagellates. In both cases the evidence is against these flagellates having any relation to the human infections.

The Mediterranean or infantile type of kala-azar, the parasite of which is commonly referred to as *Leishmania infantum*, is almost certainly transmitted by sandflies if the other forms of leishmaniasis are. In this case the only experimental evidence available tends to incriminate *P. papatasi*, but it seems that different strains of the *Leishmania* of this disease act differently in this insect. If *P. papatasi* is really the natural transmitter of both infantile kala-azar and Oriental sore, much remains to be learned as to the reasons for the different distributions of the two diseases.

Sandflies in Relation to Verruga Peruana and Oroya Fever. — The probable relation of sandflies to these diseases, which are now quite definitely shown to be different manifestations of the same infection (see p. 191), was pointed out by Townsend in 1913. The disease is limited to a comparatively small zone in the Peruvian Andes, which is inhabited by this sandfly, and it appears to be contracted at night. Townsend gave consideration to all kinds of blood-sucking insects to be found in the verruga zone. By excluding insects whose range extends beyond the verruga zone, and also day-biting insects, he reduced the probable vectors to *Phlebotomus* alone. He had so much confidence in his convictions that he named the species he found *Phlebotomus verrucarum.* Fifteen years later Noguchi and his colleagues confirmed Townsend's epidemiological evidence by injecting suspensions of crushed insects from the verruga zone into monkeys, recovering the organism of the disease (*Bartonella bacilliformis*) in pure culture, and then again producing the disease by means of the cultures. No blood-sucking insects except *P. verrucarum* and probably another species, *P. noguchii,* gave positive results, although Noguchi had previously found that the wood tick, *Dermacentor andersoni,* could experimentally transfer the disease, probably in a purely mechanical manner, and without significance so far as natural transmission is concerned.

Phlebotomus verrucarum is a species of sandfly which breeds principally in the damp recesses of the loose rubble fences which are so universally used in Peru, and probably feeds largely on a species of lizard, *Tropidurus peruvianus,* which inhabits the same rock fences. According to Townsend it requires for its life cycle a fairly high total of summer heat and much moisture, with an absence of night fogs and of low winter temperatures. The adults will not live where there are continuous strong air currents. These conditions limit the species closely to the deep-cut canyons or "quebradas," between 3000 and 8000 ft. elevation, on the west face of the Andes.

Control. — Sandflies are very difficult insects to deal with, both on account of the small size of the adults and of the nature of the breeding places.

It is not practical in warm weather to keep sandflies out of houses or beds by means of netting, since a mesh of more than 22 strands to the inch is required. When available, electric fans are excellent preventives, and almost perfect protection can usually be obtained by raising the sleeping room to a height of 12 or 14 feet above the ground; Boyd's report of officers in northwest India being bitten by sandflies on a roof 40 ft. above ground appears to require confirmation. Spraying walls, nets, etc., with solutions of formalin, cresol, or essential oils such as anise oil or eucalyptus oil, gives protection for a few hours, if one is prepared to rise in the night to renew the spraying. Personal protection can be obtained in a similar way by rubbing into the skin vermijelli, paraquit, or mosquito lotions. Townsend recommends equal parts anise oil, eucalyptus oil and oil of turpentine in a boric acid ointment. In the case of *P. argentipes* the observations of Napier and his colleagues have shown that cattle are of great value in deflecting sandflies from human beings, but as Knowles points out, the suggestion to keep a cow in one's bedroom in order to protect oneself against kala-azar is an impractical one! Natives, however, whose sleeping quarters are over cowsheds are effectively protected, as shown by the rarity of kala-azar in the parts of Calcutta where this condition prevails.

It is almost impossible to destroy sandflies in their early stages. Townsend thinks that the elimination of rubble fences in Peru would reduce their numbers, at least locally, but it would be far from a simple problem to destroy all possible breeding places, even within a very small radius. In Europe, where stone and cement are more extensively used than in America, the problem is still greater. The earthquake ruins of Sicily give unlimited breeding places. The large numbers of these insects in parts of Egypt where such places are not available indicate that damp cracks in soil may be utilized as breeding places, and it would be obviously impossible to eliminate these or to treat them thoroughly.

True Midges (Chironomidæ)

General Account. — The family Chironomidæ comprises a large number of species of small flies, sometimes almost microscopic, found all over the world. The larger ones quite closely resemble mosquitoes except for the absence of the long proboscis, and the dancing flocks of these insects which can be seen over pools or swamps on any summer day are usually taken for mosquitoes without question. As expressed by Riley and Johannsen, " these midges, especially in spring or autumn, are often seen in immense swarms arising like smoke over swamps, and producing a humming noise which can be heard for a considerable distance." In such swamps the larvæ, most of which are aquatic and live in the mud or amid aquatic vegetation, may be scooped up, literally by the shovelful. Fortunately the great majority of these insects are quite harmless, in fact, inasmuch as the larvæ are an important food for young fishes, they are distinctly beneficial. The blood-sucking species belong to the subfamily Ceratopogoninæ which is now often raised to the rank of a distinct family. They are very small, seldom over 1 to 2 mm. in length; only the females are known to suck blood. They are well known to hunters and anglers and other frequenters of the woods in most parts of the world. In America they are usually called " gnats " or " punkies " and in the West are known as " no-see-ums," on account of their very small size.

These insects (Fig. 244) can usually be distinguished from allied insects by the peculiar venation of the wings, the first two veins being very heavy while the others are indistinct. Though the bodies, and sometimes to a slight degree the wings, are more or less hairy the scales so characteristic of mosquitoes are absent. The proboscis is never long even in the blood-suckers, and one is led to marvel at the irritation which can be inflicted by such a small insect with such a small organ. As in mosquitoes the males are distinguishable by the more plumose antennæ. Usually midges rest with the front legs elevated, though not all species have this habit. In most Chironomidæ the thorax of the adult insect projects like a hood over the head, but in the subfamily Ceratopogoninæ, which alone interests us here, this is not the case, and this negative characteristic is the best distinguishing mark of the subfamily. They are distinguishable from the Simuliids by the longer antennæ and more slender bodies, as well as the wing venation.

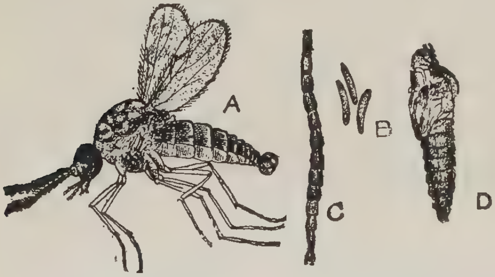


FIG. 244. Life history of blood-sucking midge, *Culicoides; A*, adult male (*C. reticulatus*), × 5; *B*, eggs (*C. marium*), × 18; *C*, larva (*C. reticulatus*), × 5; *D*, pupa (*C. marium*), × 10. (After Lutz.)

The great majority of the species which attack man and animals belong to the genus *Culicoides*, although a few species of other genera, such as *Ceratopogon* and *Forcipomyia*, have been recorded as human pests. The latter breed for the most part in damp places under bark, stones, moss, etc., out of water, and have spiny larvæ (Fig. 245), whereas *Culicoides* larvæ are unspined and more orthodox in being aquatic like the majority of the Chironomids (Fig. 244*C*). Some of the Ceratopogons suck blood from other insects, such as mosquitoes. Nearly all the blood-sucking species become active at dusk, but if disturbed many of them will bite in the shade, even on bright days. Both sexes are attracted by lights. They are much more active fliers than *Phlebotomus*, and are said to go as far as half a mile in search of a host, but only when the air is still. Most of the species appear to prefer cattle, camels, or other animals as food, but many species readily attack man.

The eggs of *Culicoides* (Fig. 244*B*), as of other aquatic midges, are deposited in gelatinous masses, like miniature masses of frog or toad eggs, being usually moored to some object. They number several hundreds. The eggs hatch in a few days, depending on temperature, and give rise to minute worm-like larvæ whose active movements caused Patton and Cragg to describe them as suggesting giant spirochætes. *Culicoides* larvæ, unlike other chironomid larvæ, do not have pseudopods on the first or last segments of the abdomen. At the posterior end there are gill-like structures which can be protruded; the larvæ do not need air as do mosquito larvæ. The food probably consists of microscopic plant and animal life or organic débris. The pupa (Fig. 244*D*) rather resembles that of a mosquito, except that the abdomen is kept extended instead of curled under, and the pupa hangs from the surface in a vertical position, breathing through a pair of trumpet-like tubes as in mosquitoes. Both larvæ and pupæ are hard to find, and the presence of a breeding place is more frequently discovered by finding the floating pupal cases from which the adults have emerged. The entire life cycle probably occupies two weeks or more, according to temperature.

Annoyance. — The amount of annoyance which may be caused by midges is sometimes very great. The writer will never forget his experiences with them in a collecting and fishing trip in the Cascade Mountains of Oregon. The midge which proved itself troublesome, a minute species of *Culicoides*, was very local in distribution, and always standing pools of shallow water were found in the near vicinity. The proximity of such pools was invariably proclaimed, towards evening, by the collection of great numbers of these insects on all exposed parts of the body, each one so minute as to be hardly visible, but in the aggregate sometimes giving the arm or shirt sleeve a dark gray color. Each one is presently the cause of an intensely itching spot. That the insects are attracted by animal smells is evident from the following experience. The writer had shot a rabbit and was skinning it. Almost immediately after the animal was cut open and the smell of the warm bowels exposed to the air I found myself attacked by myriads of these insects, and was bitten to such an extent as to be driven almost to a complete frenzy, until I discovered that only a few yards from the opened animal I was not attacked at all. The skinning of the rabbit was completed in the welcome protection of a dense smoke.

Midges as Disease Carriers. — Blood-sucking midges have been accused of transmitting a Peruvian form of dermal leishmaniasis and have been suspected as possible transmitters of kala-azar. Recently they have been proved to serve as intermediate hosts for the filarial worm, *Acanthocheilonema perstans*.

Two species of land-breeding midges, *Forcipomyia utæ* and *F. townsendi*, have been incriminated by Townsend as the carriers and intermediate hosts of the protozoan parasite causing " uta " in Peru. Uta (see Chapter V, p. 137), is a form of leishmaniasis occurring on the western face of the Andes. According to Townsend, Leishman bodies are found in the digestive tract of these midges, and injection into laboratory animals of serum containing the ground bodies of captured insects resulted in the formation of sores which Townsend regarded as uta, and from which he obtained a few Leishman bodies. Two cases are cited, also, in which uta sores developed following the bites of the midges, and supposedly due to them. According to Townsend the infection is probably transmitted by contamination of the wound made by the proboscis with infected excrement. That these insects are really the transmitters of uta in man cannot be considered as proved, but it must be regarded as a possibility.

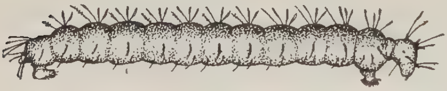


Fig. 245. Larva of *Forcipomyia specularis*. × 15. (After Malloch.)

Little is known about these species of *Forcipomyia*, but it is probable that their habits are similar to those of better known species. In the North American species the larvæ (Fig. 245) are slender whitish worms about one-eighth of an inch in length which live in damp places in moss and under bark, stones, etc. The pupæ are pale yellowish, later becoming brown.

Culicoides has been among the many insects which have been suspected in connection with the transmission of Oriental sore and kala-azar. Christophers, Shortt and Barraud found only one species, *C. macrostoma*, which would bite man in Assam; they succeeded in feeding 193 females on kala-azar patients, but only 48 survived to the third day and two to the fourth. No evidence of infection was found in any of them, in contrast to the good results obtained with *Phlebotomus argentipes*. It is therefore highly unlikely that a *Culicoides* is involved, although these insects do fit in with the epidemiological conditions.

Sharp has recently proved two species of *Culicoides*, *C. grahami* and *C. austeni* (Fig. 246), to be the intermediate hosts of the filarial worm *Acanthocheilonema perstans* (see p. 359) in British Cameroons, where about 92% of the natives are infected. Seven per cent of wild flies were found to be naturally infected. The ingested larvæ go through the usual filarial course of development in the thoracic muscles and are ready to emerge from the proboscis on the 7th or 8th day. Usually from 4 to 7 worms develop from a feeding. Only the female flies suck blood, and they feed only in darkness. Such dim light as a $\frac{1}{4}$ candle power lamp in a 7 ft. tent gives full protection, and even a full moon keeps the flies from biting. The white residents are protected by the use of nets and lights, and by the preference of the flies for black skin.

Control. — The control of the aquatic biting midges is not difficult, and can be accomplished in the same manner as can the control of swamp-breeding mosquitoes, by draining, stocking with natural enemies or oiling. It is improbable that these midges breed to any extent in transient pools, for most of them, at least, prefer pools of standing water, abundant in organic débris and microscopic organisms. The terrestrial-breeding forms of *Forcipomyia* and *Ceratopogon*, like the sandflies, are practically impossible to exterminate.

Much protection from the adults can be obtained by the use of repellents as advised for mosquitoes and sandflies (see p. 582).

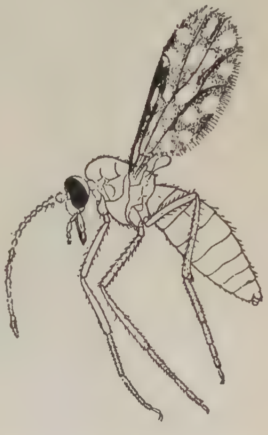


FIG. 246. *Culicoides austeni*, vector of *Acanthocheilonema perstans*. × 20. (After Sharp, from Fulleborn.)

Blackflies or Buffalo Gnats (Simuliids)

General Account. — The blackflies, as annoyers of domestic animals and man, are among the most important of insect pests. The females are most vicious blood-suckers, and in especially bad outbreaks may kill large numbers of animals. In 1923 over 3000 animals are reported to have been killed by them in Bulgaria, death being caused in from a half hour to four days. A Himalayan species, according to Alcock, has been said to kill even human beings. In Eastern Canada their attacks are frequently fatal to poultry.

These small insects, which constitute the family Simuliidæ, are quite unlike the other flies of the group to which they belong. Instead of the usual slender, long-legged, midgelike flies of this group we have in the blackflies small, robust, humpbacked creatures with short legs and broad wings, rather resembling, in a general way, miniature houseflies (Fig. 247). The antennæ are composed of 11 segments, but they are short and stocky, and have no hairs at the joints. The proboscis in the female is short but heavy and powerful, while in the male it is poorly developed.

The mouthparts (Fig. 248), consisting of toothed dagger-like mandibles and maxillæ, and also a hypopharynx and labrum-epipharynx, are very similar in general structure to those of *Phlebotomus*. Most of the northern species are black in color, whence their name, but some of the species are reddish brown or yellowish, and they may be variously striped and marked. The wings are either clear or of a grayish or yellowish color with the few heavy veins near the anterior margin often distinctively colored. Some of the species are not over one mm. in length and the largest of them scarcely exceed 4 mm.

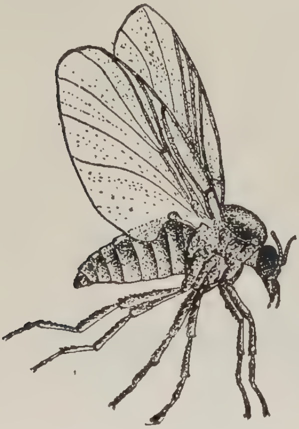


Fig. 247. Blackfly, *Simulium pecuarum*. × 7. (After Riley.)

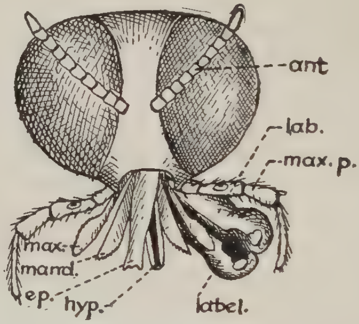


Fig. 248. Mouthparts of blackfly, *Simulium; ant.*, antenna; *ep.*, epipharynx; *hyp.*, hypopharynx; *lab.*, labium; *label.*, labellum; *mand.*, mandible; *max.*, maxilla; *max. p.*, maxillary palpus. (After Alcock.)

Life History. — Unlike the mosquitoes and midges, blackflies breed in running water and few streams flow too swiftly for them. The eggs are laid in large masses, up to many thousands in number, by a number of females. The eggs (Fig. 249*A*), which are elliptical and yellowish and have a peculiar slimy coating, are deposited by some species on leaves or blades of grass which are occasionally licked by running water, the weight of the eggs sufficing to submerge them; other species dart into the water and deposit directly on the slimy surfaces of submerged stones or twigs. The writer found a favorite breeding place of the blackflies in the woods of northern Ontario (species undetermined) to be on the slimy boards of old lumber chutes over which water was constantly flowing. It requires at least a week for the eggs to hatch.

The larva (Fig. 249*B*), as soon as hatched, attaches itself to a stone or other submerged object by a sucker-like structure armed with rows of hooklets at the posterior end of the body. The hooks hold fast to silken threads spun by the larvæ. As expressed by Alcock, " one of the most characteristic attitudes of the larva is to sit upright on the end of its tail, — to use the language of the poets of the daily press, — with its mouth fans standing out from its head like a pair of shaggy ears." The "mouth fans," which are very delicate and elegant, are used for sweeping microscopic particles into the mouth as they are brought by the running water. The stump of a leg on the first segment (Fig. 250, *prol.*) is used for creeping, in conjunction with the posterior sucker, the larva looping along like a "measuring worm"; it is also of use in constructing the silken cocoon from the secretions of the salivary glands. This single little leg has a crown of tiny hooklets which make it possible for the possessor to hold its ground even in a torrent of water. The salivary glands referred to are quite unlike those of other insects, in that they extend clear back to the posterior end of the body (Fig. 250, *sal. gl.*).

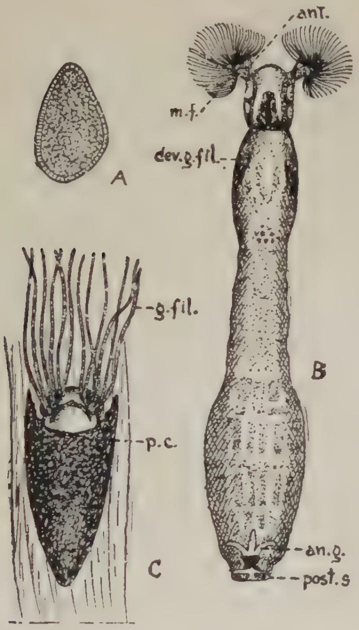


FIG. 249. Developmental stages of blackflies. *A*, egg of *Simulium venustum; B*, larva of *S. bracteatum; C*, pupa (in pupal case) of *S. venustum;* all much enlarged, not drawn to same scale; *an. g.*, anal gills; *ant.*, antenna; *dev. g. fil.*, developing gill filaments of pupa; *g. fil.*, gill filaments; *m. f.*, mouth fans; *p. c.*, wallpocket-like pupal case; *post. s.*, posterior sucker. (*A*, after Mecznikow from Jobbins-Pomeroy, others after Jobbins-Pomeroy.)

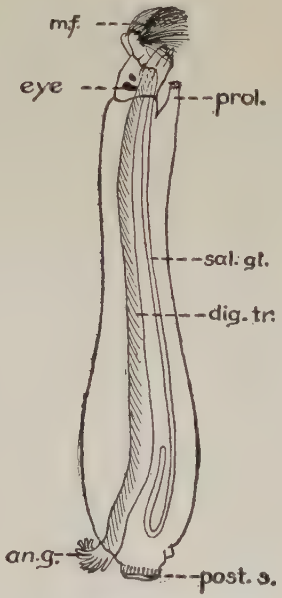


FIG. 250. Larva of blackfly, *Simulium venustum*, side view showing some of internal anatomy; *an. g.*, anal gills; *dig. tr.*, digestive tract; *m. f.*, mouth fans; *prol.*, proleg with sucker and hooks; *post. s.*, posterior sucker; *sal. gl.*, salivary and spinning gland.

The fluid secreted hardens to silk at once on exposure to water, and is used not only in spinning the cocoon, but also in spinning anchoring threads and life-lines. According to Malloch, the larva when disturbed releases its hold and floats downstream, holding by the stumpy leg to a silken thread which is being spun out, and by means of which the insect later regains its former position. The larvæ breathe by means of tiny gills which can be projected through a slit in the last segment of the abdomen (Figs. 249 and 250, *an. g.*). The larvæ are never found solitary, as would be expected from the manner of laying the eggs; the writer has seen the boards on the bottom of a log chute completely covered with mosslike patches of these larvæ for areas of a square yard or more.

After four or five weeks, in summer, the larvæ prepare to go into the resting pupal stage, and spin for themselves a partial cocoon which is variously shaped like a jelly glass, slipper, wall pocket, etc., open at the upper end for the extrusion of the branching gill filaments which are used as breathing organs (Fig. 249*C*). Some species simply spin a snarl of threads, the work of a whole community, in the meshes of which the pupæ exist in a fair state of protection. The general form of the pupæ can be seen in Fig. 251. The breathing filaments vary greatly in different species and may have from four to 60 branches.

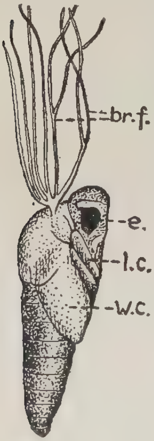


Fig. 251. Pupa of blackfly, *Simulium jenningsi*, removed from case; *e.*, eye; *l. c.*, leg cases; *br. f.*, breathing filaments or gills; *w. c.*, wing case. (After Jobbins-Pomeroy.)

The adults escape from the pupæ after from one to three weeks through a slit in the back, and are carried safely to the surface by a bubble of air which has been collected inside the old pupal skin. The adults are short lived and lay their eggs soon after emergence. The whole life of a generation from egg to egg may be passed in from six weeks to two months or more. Some species have several generations a year but some produce but a single brood a year. The Canadian species already referred to is seen only for a few weeks in May and early June, during which time it is locally excessively abundant. Most if not all of the species hibernate in the larval stage. In some species, at least, it appears probable that after the spring brood has appeared and streams are low, eggs are laid in situations where they remain dry over summer, to hatch with the coming of high water in the fall, and to emerge as adults in the following spring. The adults of at least some species are not as closely confined to their breeding places as are many Diptera, but may travel a mile or more, and possibly a number of miles. Most species are diurnal, but the writer found the Ontario species to be most active from late afternoon until dark, and again early in the morning. This species will also bite readily at night in the presence of artificial light.

The species of blackflies are numerous, but are all included in the single genus *Simulium*, with several subgenera which some workers elevate to the rank of true genera. Some species do not attack man but viciously attack various domestic animals. While on a collecting trip in the Cascade Mountains of Oregon the writer found it necessary to keep the pack animal picketed in the smoke of the camp fire constantly to protect the poor creature from the blackflies which congregated in large numbers about his eyes and nose, yet neither the writer nor his companion was ever bitten by one of these flies. One of the most troublesome species in the United States is *S. pecuarum*, the famous buffalo gnat of the south central portion of the country. This species was formerly more abundant than now, and was a terrible scourge to mules and cattle. *S. venustum* is one of the most important molesters of man. It occurs over the greater part of the eastern portion of North America.

Annoyance. — In the estimation of the writer, no insect scourge he has ever experienced is more terrible than an attack of blackflies as he encountered them in Canada. From accounts of other authors they must be equally terrible in other places. King, for instance, states that in parts of Sudan (Dongola) a species known as the nimetti, *Simulium griseicollis*, renders life a burden during the winter months. The famous Columbacz fly, *S. columbaczense*, of southern Europe is said to be a terrible pest, and there are instances of children having been killed by it. My own experiences occurred in the woods of northern Ontario early in June. The flies were at the height of their short season, and made the lives of man and animals almost unbearable. It was with some impatience (having been bred among the mosquitoes of New Jersey) that I submitted, on first arrival, to the precautions recommended to keep the flies from being able to bite, and my carelessness resulted in many individuals of the fearful swarms of flies getting through my armor. The resulting bites, which bled at first, were only slightly painful to begin with, but became progressively more swollen and more agonizingly itchy for three days, when the bites became oozing pimples. Accompanying this there was a feeling of general " ennui " and despondence with some fever, due, no doubt, to the action of the poison injected by the numerous insects. Subsequent attacks by the flies, though always far from pleasant, were not so severe in their effects, a certain amount of immunity apparently having been built up. On account of the slow development of the symptoms it was my belief that possibly they were due to the injection of a living organism. Stokes, however, has shown that the effects of blackfly bites, essentially as described above, can be reproduced by the injection of material from preserved flies. An interesting suggestion is made by Stokes that possibly the first bites of the flies sensitize the body to the particular poison injected so that it reacts rather violently to subsequent injections of it in an anaphylactic manner. Possibly the rashes produced by mites, lice, etc., may also be due to such a reaction.

***Simulium* and Disease.** — The first definite instance of the involvement of *Simulium* in the transmission of disease was discovered by Blacklock (1926). He showed that in Sierra Leone a species of this genus, *S. damnosum*, serves as an intermediate host for the filarial worm, *Onchocerca volvulus*. In the region where the work was done as high as 45% of the natives were found to have the microfilariæ of this worm in their skins, but not in the blood. *Simulium* takes some little time to rasp a hole through the skin before it can draw blood, thereby probably dislodging or stimulating the worm embryos. Flies fed on infected areas of skin obtain large numbers of embryos in their guts. In one experiment 80% of the fed flies had embryos in their stomachs, in some cases from 100 to 200 of them. The larvæ subsequently go through a development in the thoracic muscles of the fly, invade the head, and spontaneously leave the head or the proboscis when brought in contact with warm serum. For further details see p. 362.

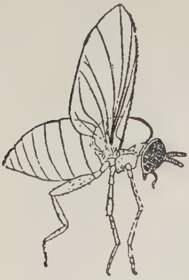


Fig. 252. *Simulium damnosum*, vector of *Onchocerca volvulus*. (After Blacklock, from Fulleborn.)

Simulium damnosum (Fig. 252) is a species which is widely distributed in equatorial Africa, from Sierra Leone to Uganda and the head waters of the Nile; it is uniform black, with golden hairs on the thorax. It breeds in large flowing rivers, and is very abundant along their banks, where there is high grass or dense vegetation to protect it from wind. The young stages occur attached to rocks and submerged vegetation. It is active from 6 A.M. to 6 P.M., but in bright sunlight it bites only where shaded, usually not above the level of the top of the grass, and will only go one or two yards. On dull days it travels further, and bites more actively. Natives, who use the edges of streams as latrines, are badly bitten by it; frequently septic sores develop at the site of the bites.

Some years earlier it was suggested by Robles that *Simulium samboni* and *S. dinelli* were probable transmitters of *Onchocerca cæcutiens* in Guatemala; this probability seems now very likely to prove true. If it is found that a *Simulium* is also the transmitter of *Onchocerca gibsoni* in Australia, which causes enormous injury to cattle skins, there may be some hope of controlling the disease and reducing the loss.

Simulium has also been suggested as a likely vector of a forest type of leishmaniasis in Paraguay and Brazil; natives in endemic areas believe that blackflies cause the infection and that rattlesnakes, on which the flies feed, serve as a reservoir of infection. This is reminiscent of the case of geckos, *Phlebotomus minutus*, and Oriental sore (see p. 133), and is hardly more likely to prove true.

Some years ago a theory was rampant that blackflies were the transmitters of pellagra, but since it is now fairly generally accepted that pellagra is due to a vitamin deficiency in the diet, or is at least associated with inadequate diets, blackflies as well as other blood-sucking insects have an excellent alibi, and can scarcely be involved.

Control. — Since blackflies breed in running water the methods to be employed in their extermination are quite different from those ordinarily used in the extermination of mosquitoes. One of the measures most widely used is the treatment of breeding streams with phinotas oil, a poisonous oil which forms an emulsion in the water and slowly soaks through it. O'Kane has reported successful results with a miscible phinotas oil, in such concentration as to make the water milky white, and in sufficient amounts so that the cloudy water requires at least 90 seconds to pass a given point. There is only a narrow margin between the minimum treatment which will kill blackfly larvæ and the maximum that fish can endure, therefore only short sections of a stream should be treated on a given day, allowing time for a thorough clearing of the stream before the next application. Often the breeding grounds of blackflies may be locally destroyed or reduced by damming the stream at intervals, leaving falls between, or in the case of small brooks by the construction of underground channels or of a drain-pipe line. In some cases sweeping of stones, etc., with brooms may be of help. The clearing away of roots and fallen logs from streams is often of value, in that it removes surfaces on which the eggs are laid, and obliterates the numerous small falls which are ideal for the larvæ. In larger streams the cultivation of fishes, such as trout, young bass, darters, etc., greatly reduces the number of blackflies if it does not eliminate them entirely. In such cases care should be taken that there are no small trickling streams which are not readily reached by fish.

A considerable degree of protection from blackflies can be obtained by the use of repellents such as are used for mosquitoes, but their efficiency seems to be lost more quickly than in the case of mosquitoes. Moreover the crawling habits of the flies must be taken into account, and other parts of the body than those which are directly exposed must be treated. Blackflies may be driven from houses by fumigation with pyrethrum powder or by any other fumigation method. In camp life the use of smudges is indispensable. An efficient smudge which will last all night can be made in an old bucket with a few holes punched near the bottom. A small fire is started in this and then the bucket is filled with partly wet, punky, decayed wood which will smoulder slowly and produce a dense yellow smoke. Sleeping in the presence of such a smoke is at first almost as unpleasant as are attacks by mosquitoes and black-flies but one soon becomes accustomed to it, and it has none of the terrible after-effects of an attack by the flies.

Horseflies (Tabanidæ)

General Account. — Although primarily of importance as bloodthirsty pests of domestic animals, the gadflies or horseflies (Tabanidæ) cannot be ignored as biters of human beings, especially as they have been shown to be implicated in the spread of certain human diseases. The bites are painful, and sometimes cause annoyance for several hours; not

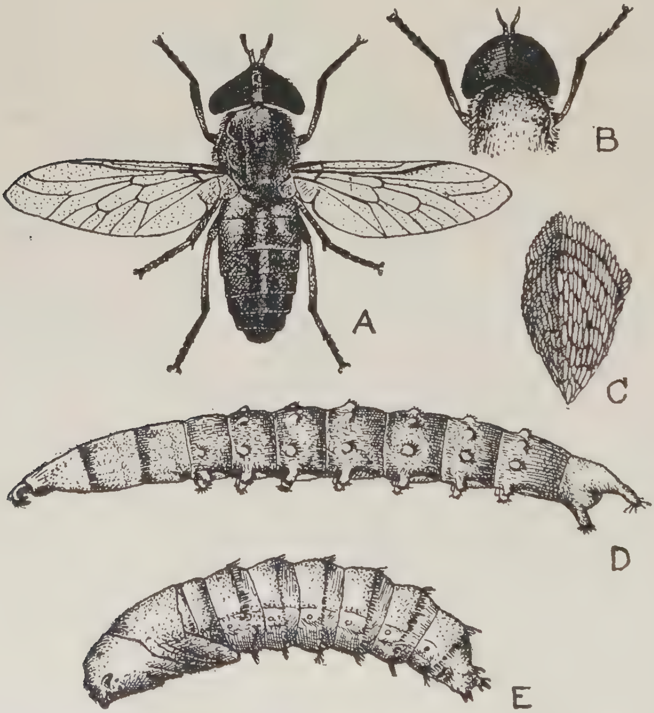


FIG. 253. Life history of a Tabanid, *Tabanus kingi*, a "seroot" of Sudan. *A*, adult female, × 3; *B*, head of adult male, × 3; *C*, egg mass, laid in crevices of rock, × 5; *D*, larva, × 2½; *E*, pupa, × 2½. (After King.)

infrequently these bites, which may bleed, subsequently become infected and give rise to troublesome sores. The females alone are bloodsuckers, the males living chiefly on plant juices, in fact even the females in some genera feed on flowers. These flies, of which over 2500 species have been recorded, occur in every part of the world, and in every sort of habitat where water or damp places are available for breeding purposes.

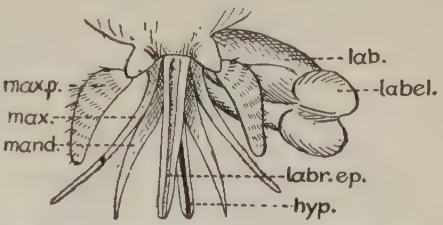


FIG. 254. Mouthparts of a tabanid; *hyp.*, hypopharynx; *lab.*, labium; *label.*, labellum; *labr. ep.*, labrum-epipharynx; *mand.*, mandible; *max.*, maxilla; *max. p.*, maxillary palpus.

The tabanids are of large size and heavy build (Fig. 253*A*). They are often beautifully colored in black, brown and orange tones, sometimes with brilliant green or green-marked eyes, though in most species of temperate climates the huge eyes are brown or black. The head is large, and in the male is almost entirely occupied by the eyes, which meet across the crown of the head (Fig. 253*B*), though in the females a narrow space is left between them. The antennæ are of characteristic shape (Fig. 237*C*) varying somewhat in the different genera.

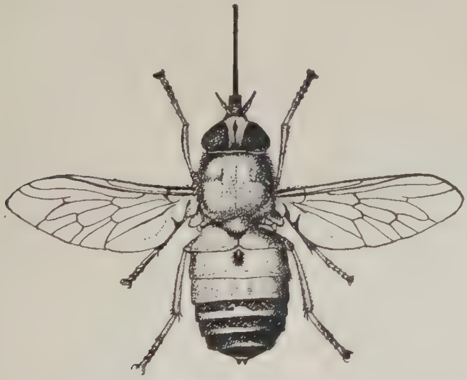


FIG. 255. A long-beaked tabanid, *Pangonia ruppellii*, of eastern Africa. × 2. (After Castellani and Chalmers.)

The mouthparts (Fig. 254) are almost exactly like those of the blackflies on a large scale. The stabbing and cutting parts are usually short, heavy and powerful, though in one genus, *Pangonia*, the proboscis is very long, enabling the fly to pierce even through thick clothing. Most of the species are very deliberate and persistent in their feeding and are not easily disturbed when they have begun to suck blood. The thorax is relatively long, and the wings are large and expansive and usually held at a broad angle to the body, as shown in Fig. 256. The markings of the wings usually give the easiest means of identification of the genera. Of the four most important genera as human pests, *Tabanus* (Fig. 253), is of large size and has clear or smoky wings, with no spots or a few small scattered ones; *Pangonia* (Fig. 255) also has clear or smoky wings but can be distinguished by the long proboscis; *Hæmatopota* is of moderate size and has wings with profuse scroll-like markings; and *Chrysops*, the species of which are often small, even smaller than a housefly, has a conspicuous black band on the wing (Fig. 256).

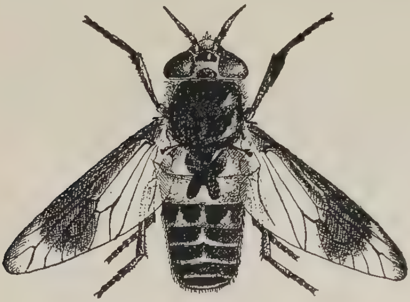


FIG. 256. A deerfly, *Chrysops callidus*. × 4.

Life History. — All the tabanids breed in water or in damp places. The eggs (Fig. 253*C*), several hundred in number, are laid in definitely shaped masses on the leaves of marsh or water plants, on the leaves or twigs of trees overhanging water, or in crevices of rocks along the sides of streams. Many species select particularly species of plants on which to deposit eggs. The eggs are white when laid, but soon turn dark. They are deposited during the summer and under favorable circumstances hatch in from four to seven days. Many are attacked by small hymenopteran parasites. The newly hatched larvæ fall into the water or to wet ground or decaying vegetation such as occurs around the edges of marshes, in sphagnum bogs, in decaying logs, etc. The larvæ (Fig. 253*D*) are cylindrical legless creatures, pointed at each end, and with a number of spines or warts on the body. They are voracious feeders and prey upon various soft-bodied animals which they find in the water or mud in which they live, and are not averse to the practice of cannibalism if food is scarce. The larvæ grow rapidly during the remainder of the summer, but remain inactive and with little or no growth during the winter. In the spring they complete their development and creep out to drier ground to pupate. The pupa (Fig. 253*E*) often resembles the chrysalis of a butterfly in form. The adults of the species of temperate climates emerge after two or three weeks, but King states that tabanids in the Sudan exist as pupæ only six to eight days. The whole life history of species of temperate climates therefore occupies about a year, but it is shorter in tropical species, in which there are probably several broods a year.

The adult flies are strictly diurnal, and are often active in the clear sunlight of a summer day, though many forest-dwelling forms, *e.g.*, the deerflies, *Chrysops*, prefer shade. They do not go in swarms as do many other biting insects but are usually solitary in habit. On account of their powerful wings they are sometimes found at considerable distances from their breeding places. Gadflies collect near pools and skim over the surface of the water, the under side of the body often touching the water. Portchinsky, in Russia, has devised a means of trapping the flies, based on this habit (see p. 531).

Tabanids and Disease. — Tabanids are of importance in connection with the transmission of some of the trypanosomes of animals. *Trypanosoma evansi*, which causes surra in horses, cattle, camels, dogs, etc., is undoubtedly commonly transmitted by tabanids. Many investigators have proved that the disease can be transmitted in a mechanical manner by the soiled proboscis of flies which have had interrupted feeds, *i.e.*, began their meal on one animal and finished it on another. In Java, *Tabanus striatus*, which breeds commonly in rice fields, is a particularly important vector. El Debab of camels in North Africa, caused by the closely related *T. soudanense*, is apparently transmitted in a similar manner. In French Indo-China the closely related *Trypanosoma annamense* is believed to be transmitted from wild buffaloes to cattle by forest tabanids, and then to be transmitted among domestic animals mainly by the stable-fly, *Stomoxys*. In many parts of the world cattle are infected with an apparently harmless trypanosome, *T. theileri* or closely related forms, which are not only mechanically transmitted by tabanids, but undergo a developmental cycle in the fly. Nöller has succeeded in producing infection in cattle by inoculating cultures made from tabanids infected with "*Crithidia subulata*" thus proving that this really is identical with the trypanosome; whether such a cycle of development can occur in the case of surra remains to be proved. It has also been shown that *Trypanosoma brucei*, causing nagana in animals, can be mechanically transmitted by inter upted feeding of tabanids, as well as *T. equinum*, causing mal-de-caderas, and *T. equiperdum*, causing dourine. There is, therefore, little doubt but that the trypanosomes of human sleeping sickness may also occasionally be transmitted in this manner, though the danger cannot be considered very great in this case. The frequency with which tabanids, annoyed by a swishing tail, fly to other animals to continue a feeding makes them especially good mechanical transmitters

Another important disease disseminated by tabanids is anthrax. This is a bacterial disease to which nearly all herbivorous animals and man are susceptible, and which is very destructive, sometimes killing over 75% of its victims. The bacilli which cause the disease gain entrance to the body either through abrasions of the skin to the blood, through spores in the air to the lungs, or through contaminated food to the intestine. The bacilli have been found in the alimentary canal of tabanids which have fed on dying or dead victims, and animals inoculated with these bacilli died of anthrax. That these flies could transmit the disease not only when crushed so that the contents of the digestive tract could contaminate the wound, but also by their bites, has been stated many times, and has been observed in China under conditions which placed it beyond doubt. The method of transmission is purely mechanical and probably occurs only when a fly which has been feeding on a diseased animal finishes its meal on a healthy animal or on a human being, the disease germs adhering to the mouthparts long enough to be transferred to the new animal. The stable-flies, *Stomoxys*, and other biting flies which will attack two or more animals in quick succession are equally as dangerous as anthrax carriers.

Tabanids have often been accused of causing diseases similar to, if not identical with, Oriental sore. In the intestines of various tabanids there exist flagellate parasites of *Herpetomonas* or *Crithidia* type. The latter have been shown to represent cattle trypanosomes, however. Whether other flagellate parasites of tabanids, when injected into a human skin, can cause *Leishmania* infections is at present largely a matter of speculation. Obviously such implanted parasites would be permanently side-tracked, and would stand little chance of ever being released by a fly of the species in which they normally live. Such a theory is proposed to explain the sporadic cases of leishmaniasis of the skin which occur in Panama and other places, and which are usually reported to develop at the site of a horsefly bite. In São Paulo, Brazil, a form of leishmaniasis is very common among forest workers, even in wild uninhabited regions. The fact that the disease is contracted only by men who spend the day in the forest, and is most prevalent in May and June, a time corresponding to the appearance of many tabanids, points strongly to these insects as the carriers of the infection, since they are the only diurnal insects exclusively found in forest regions. The forest leishmaniasis of Paraguay may also be due to tabanids.

In one other case a tabanid is implicated in the spread of a disease. In the tropical jungles of Africa certain species of *Chrysops*, locally known as mangrove flies, serve as intermediate hosts for filarial worms. Leiper and other investigators have found that the larvæ of the loa worm, *Loa loa*, which swarm in the peripheral blood of the host in the daytime only, undergo rapid development in several *Chrysops*, especially *C. dimidiatus* and *C. silaceus* (see p. 358).

It has recently been shown by Francis that tularemia, a rodent disease of western United States, caused by *Pasteurella tularense*, and transmissible to man, may be transmitted, and probably commonly is, by the deerfly, *Chrysops discalis*. These flies are infective from a few seconds to at least fourteen days after biting an infective rabbit.

Control. — Prevention of bites from tabanids, especially during an epidemic of anthrax, or where diseases which may be transmitted by tabanids are prevalent, is important. Practically the only means that can be employed is the use of repellents, as for other insect pests (see p. 581). According to Herms, repellents efficient against tabanids usually contain fish oil.

Portchinsky, a Russian entomologist, having found that tabanids have the peculiar habit of skimming over pools, touching the lower side of their bodies to the surface, advised the conversion of such pools into traps by pouring oil on them to produce a surface film, so that the insects would be caught in it, and the spiracles closed up. In an experiment which he performed in a pool with a surface of a little over a square yard, he caught in five days 1260 male and 258 female *Tabanus*, and 416 male and 33 female *Chrysops*. This "pool of death" was literally studded with "floating islands of dead tabanids." The flies are said to visit the pools even after sucking blood. Portchinsky suggests the construction of traps of this nature in pastures where tabanids are troublesome, fencing them in, of course, to prevent the stock from getting access to them.

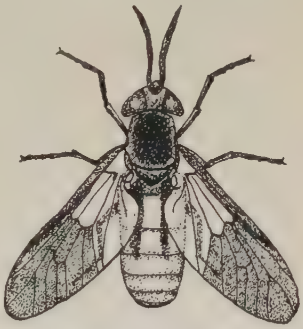


Fig. 257. *Chrysops dimidiatus*, vector of *Loa loa*. (After Grünberg, from Fulleborn.)

From the solitary nature of the flies, and the great variety of breeding places which may be selected, it is obviously impossible, in most cases, to exterminate tabanids during their early stages. Natural enemies probably do much to limit their numbers; fishes and large carnivorous aquatic insects prey upon the larvæ, and birds and hornets on the adults. Hine describes seeing bald-faced hornets, *Vespa maculata*, capture and cut to pieces horseflies which were too large for them to carry. In Java a bird, *Bulbulculus coromandus*, which swarms in rice fields, does good service in destroying tabanids. In one case 40 flies were found in a single stomach. Hymenopteran parasites which attack the eggs also help to keep down their numbers.

Tsetse Flies

We pass now from the suborder Orthorrhapha to the other suborder of Diptera, the Cyclorrhapha, which are distinguished by having larvæ without distinct heads, and by the fact that the adults escape from the pupal case by a circular opening in the head end. As already noted all the species of this suborder which suck blood from man belong to the family Muscidæ, which includes the common housefly and many other non-blood-sucking flies as well as the biting species, such as the stable-fly, *Stomoxys*, and the tsetse flies, *Glossina*.

Next to the mosquitoes the tsetse flies are the most important of the biting flies. The history and destiny of the African continent has been and will be very largely controlled by these insects. As far as their own biting power is concerned, tsetse flies are of little importance; their bites are less painful than are those of many other biting flies of similar size. It is in the rôle of carriers of trypanosome diseases that they gain their importance. Not only human sleeping sickness, but also a large number of deadly trypanosome diseases of animals are transmitted by these insects. The native wild animals of Africa are largely immune to these diseases and serve as a reservoir for them, but domestic animals and man succumb in large numbers, in fact to such an extent that some parts of Africa are uninhabitable, and in other parts it is impossible to keep domestic animals of any kind. The abundant and varied wild game of Africa, particularly the numerous species of antelopes, are the chief natural source of food for tsetse flies, and since the flies serve as intermediate hosts for the trypanosomes harbored by the wild game, it is obvious that when man or domestic animals are bitten by these flies they are in great danger of being inoculated with one or more species of trypanosomes.

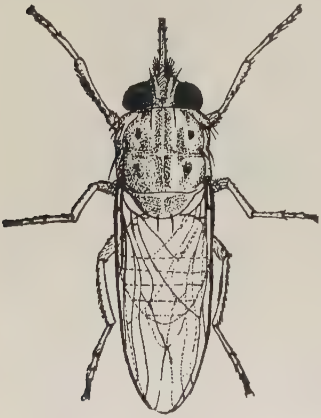


Fig. 258. Tsetse fly in resting position. × 4. (After Austen.)

General Form. — The tsetse flies (Fig. 258) are elongate, dark brown or yellowish brown flies, some species no larger than an ordinary housefly, others larger than blowflies. They are usually included as an aberrant group of the housefly family, Muscidæ, but from other members of the family they differ in a number of striking ways, especially in the manner of reproduction, and in form of the larva. They constitute the genus *Glossina* which contains 15 species and has no very close allies; some species are of very wide distribution, while others are local or very rare. Tsetses can most easily be distinguished from other flies by their position when at rest (Fig. 258); their wings are folded flat, one directly over the other, straight down the back, like the blades of a pair of scissors, while the proboscis projects horizontally in front of the head. Beyond these characteristics there is nothing strikingly distinctive about a tsetse fly, and it is therefore difficult for anyone who is not thoroughly familiar with it to identify it on the wing. The darting manner of flight and buzzing sound are said to be quite diagnostic when one is once familiar with them. When the flies are caught and examined, however, there are a number of good identification marks. Most characteristic, perhaps, is the arrangement of the mouthparts and antennæ (Fig. 259). The proboscis consists of a bulblike base which is continued as a slender shaft, composed of a grooved lower lip with two needle-like puncturing organs within it, one of which, the hypopharynx, contains a delicate tube for carrying the salivary juices. The proboscis proper is ensheathed in the maxillary palpi which are so grooved as to conceal entirely the mouthparts when the latter are not in use, and it is thus the palpi alone that are seen when the long blunt-tipped proboscis is observed. The characteristic form of the antennæ is shown in Fig. 259. The thorax is relatively large and quadrangular, with a characteristic pattern which is, however, inconspicuous in some species. The abdomen may be nearly uniform dark brown, or pale brown banded with a dusky color. The male has a large oval swelling on the under side of the last segment of the abdomen, the "hypopygium" (Fig. 260), which forms a good distinguishing mark between the sexes.

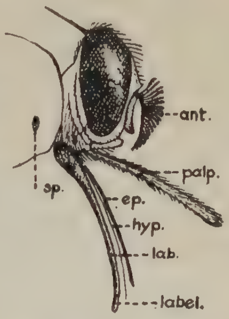


Fig. 259. Head and mouthparts of tsetse fly; *ant.*, antenna; *ep.*, epipharynx; *hyp.*, hypopharynx; *palp.*, palpus; *lab.*, labium; *label.*, labellum; *sp.*, spiracle. (After Alcock.)

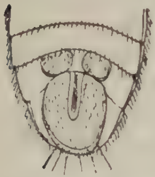


Fig. 260. Hypopygium of male tsetse fly. (After Alcock.)

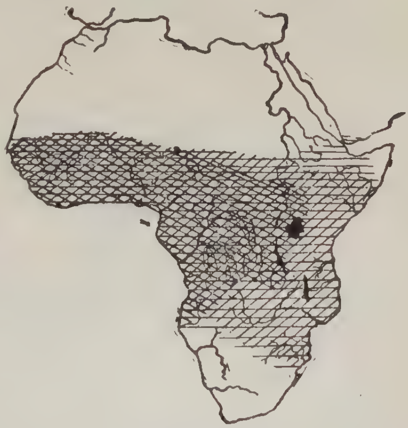


Fig. 261. Approximate ranges of tsetse flies. (Compiled from Austen.)
≡ . . . range of entire genus *Glossina*
\\\ . . . range of *G. palpalis*
/// . . . range of *G. morsitans*

Distribution, Habits, etc. — Tsetse flies, fortunately, are limited in their distribution to the middle portion of the African continent from south of the Sahara Desert to the northern borders of British South Africa (Fig. 261, ≡). One species occurs in the southwestern corner of Arabia. Tsetses are by no means evenly distributed over this great area, but are limited locally to "fly-belts," chiefly along rivers and at the edges of lakes. All the factors which cause the "patchy" distribution of tsetses are not known; there are cases where close limitation to certain areas cannot be explained by any known requirements of the flies. In Nigeria it has been observed that in the South, where the annual rainfall exceeds 50 inches, tsetses are practically continuous in distribution, whereas in the drier northern areas they occur chiefly in the vicinity of water-ways. Different species vary in their choice of habitats; *Glossina palpalis* (Fig. 266) and *G. tachinoides*, the carriers of Gambian and Nigerian sleeping sickness, are seldom found more than 30 yards from the edge of water where a sandy bottom and overhanging vegetation is abundant, though they follow animals and man for a few hundred yards from such positions. These species are found only in shady and fairly humid places. *Glossina morsitans* (Fig. 267), the fly which is particularly well known to big-game hunters in Africa and is the carrier of Rhodesian sleeping sickness, is less dependent on water, and in fact prefers a rather hot and fairly dry climate. It is confined to open brushy country with scattered trees, where there is a moderate amount of shade for cover. It is never found either in dense forest or in open grass land. Most other species of tsetses resemble one or another of these species in choice of habitats, though few if any are as independent of water as is *G. morsitans*.

There is considerable evidence that tsetse flies are more or less migratory in habit. On the African Great Lakes they have been observed to make regular movements along the lake shores, and in many localities in West Africa, when the hot parching winds known as the "harmattan" blow from the interior, they forsake the smaller water courses, where both water and vegetation soon dry up, and concentrate along the borders of larger bodies of water. They likewise migrate north or south with the advent of wet or dry seasons, and sometimes move over considerable distances with herds of wild animals.

Tsetses are diurnal in habits, but the time of activity varies with the species. *G. palpalis* is most active during the middle part of the day on bright days; *G. tachinoides*, on the other hand, is especially hungry on dull days and early in the morning; *G. morsitans* is active in the morning and afternoon, but usually disappears at midday; *G. brevipalpis* and *G. longipennis* bite in the early morning from sunrise until about 8 A.M. and in the afternoon from 4 P.M. until some time after dark. Both the last-named species are attracted by lights at night, and enter lighted railroad coaches passing through the "fly-belts." *G. palpalis*, and probably other species also, seldom rise more than a few feet above the ground.

All of them seem to be guided to sheltering trees and food animals by sight, and can be attracted by dummy animals standing in conspicuous places. Moving objects also attract them.

It has been the universal experience of collectors of tsetse flies that the males outnumber the females, often to the extent of ten or more to one. Yet it is a remarkable fact that when bred in the laboratory, males and females are obtained in equal proportions. Many different explanations for these apparently contradictory facts have been proposed, but the most probable is the one recently brought out by Lamborn, based on his observations on *G. morsitans* in Nyasaland. Lamborn has observed that copulation takes place after a rough capture, and that, in captivity at least, females even in an advanced state of gestation are not exempt from the attacks of the males, although this often results in abortion. In nature, therefore, the pregnant females would necessarily have to hide to avoid the males, and so would be less likely to be caught by a casual collector.

Tsetses show marked preference for certain colors, being especially attracted to blacks or browns, and repelled by white. The dark skin of negroes is selected in preference to pale skin to such an extent that a white man is seldom troubled when accompanied by natives. Black or dark clothes are preferred to light ones; khaki color, however, appears to be particularly attractive to them.

Unlike most blood-sucking Diptera, both sexes of tsetse flies are blood-suckers. When biting they spread apart their front legs, lower the proboscis into the skin and begin to gorge. The abdomen of an unfed tsetse is very flat (Fig. 262*A*) but after 30 or 40 seconds of feeding it becomes distended like a balloon, sometimes containing over twice the weight of the fly in blood (Fig. 262*B*). The flies do not feed exclusively on blood, but also suck plant juices and show definite, selective taste for various fluids presented to them under a membrane, according to experiments by Yorke and Blacklock. There is a difference in the various species with respect to the tastes in blood. *Glossina morsitans* and *G. pallidipes* are much more dependent on mammalian blood than is *G. palpalis* or *G. tachinoides*, and under normal conditions seldom take

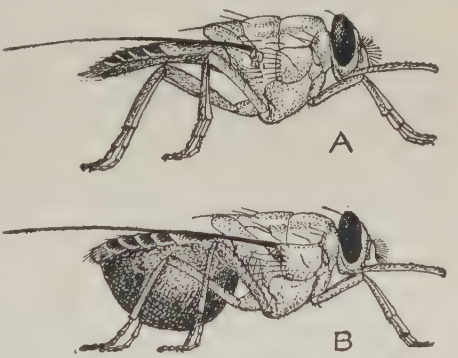


Fig. 262. *Glossina morsitans* before (*A*) and after (*B*) feeding. × 4. (After Austen.)

other blood, and then apparently only avian blood. For this reason *G. morsitans* is very dependent on large game or domestic animals, and rapidly falls off in numbers, and shows evidences of starvation, when deprived of such food. Although there is then an increase in the percentage feeding on human blood, it seems that the food deficiency cannot be made up at human expense. Small mammals cannot be utilized on account of their retiring and nocturnal habits. In some localities in Congo it seems that, although this species also attacks man and domestic animals when an abundance of game is present, when these animals are eliminated it is no longer able to maintain itself in spite of increased numbers of both man and domestic animals. No doubt concomitant changes due to cultivation and clearing, with effects on the breeding and hiding places, are here involved more than the suitability of the food. The relative extent to which *G. morsitans*, *tachinoides* and *palpalis* suck blood of ungulates is further demonstrated by the relative frequency of developing mammalian trypanosomes in them, which is in the proportion of about 4 : 2 : 1 respectively. *Glossina palpalis* and *G. tachinoides*, on the other hand, are much less discriminating, and feed freely on any available blood, even of reptiles and amphibians; in fact *palpalis* often subsists largely on crocodiles and large lizards. Nevertheless these species, too, decrease in numbers with the elimination of big, game but there is much less evidence of starvation, and there is little reason to believe that they would cease to exist even where the fauna is reduced to the possible minimum; *tachinoides* seems to make ends meet even where man is the only available host. The habit of many species of frequenting places where game animals come to drink or browse, and of feeding early in the morning or at evening seems to be an adaptation to the habits of these large mammals.

Life History. — Tsetse flies differ from all others of their family in their remarkable manner of reproduction. Not only do they not lay eggs, but the single developing larva is retained within the body, being nourished by special glands on the walls of the uterus. The larva is full grown and occupies practically the entire swollen abdomen of the mother before it is born. The process of giving birth to the larva is very rapid, occupying only a very few minutes. As soon as born another larva begins its development, etc. In *Glossina palpalis* the first larva is born three or four weeks after mating, immediately after emergence from the pupal case, and another is born every nine or ten days providing the temperature is around 75° or 80° F. and food is abundant. There is little data on the total number of young produced, but in one captive fly eight larvæ were produced in 13 weeks and only one egg was found left in the body. Pregnant flies often abort when disturbed and cases are known in which the larvæ pupated within the abdomen of the mother, to the destruction of both of them.

The larva (Fig. 263) is a yellowish white creature, about 8 to 10 mm. in length, with a pair of dark knoblike protuberances at the posterior end of the body between which are the respiratory openings. It immediately hides itself at a depth of 1 to 2 cm. in loose soil or under dead leaves in the place where it was deposited by the mother, and transforms to a pupa (Fig. 264). The pupation takes place in the course of less than half an hour in soft dry ground, and in an hour to an hour and a half in hard or damp ground. After pupation the color begins to turn dark and in four hours the pupa is a dark purplish brown color. It is shaped more or less like a small olive, and has at the tip of the body the blackish knobs which are so characteristic of the larval stage also. The shape and size of the knobs and of the notch between them are good distinguishing marks between species. The duration of the pupal stage depends on the dryness of the soil, temperature, exposure to sunlight, etc., and may occupy from 17 days to nearly three months. In experiments made by Lloyd with *Glossina morsitans* the pupal stage ranged from 23 days at 85° F. to 81 days at 70°. Few adults emerged at temperatures below 70° or above 86°. Little is known about the reproductive season, but it is probable that reproduction occurs only in the warm part of the dry season in cool climates, but may occur to a varying degree throughout the year in hot climates.

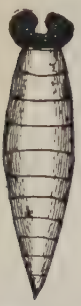


FIG. 263. Newly born larva of tsetse fly, *Glossina palpalis*. × 5. (After Roubaud.)

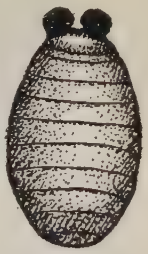


FIG. 264. Pupa of tsetse fly, *Glossina palpalis*. × 5. (Partly after Austen.)

The places where the pupæ are found vary somewhat with the species, but all species select dry, loose soil in shaded, protected spots, preferably in places where a little sunlight penetrates for a short time each day. *G. palpalis* deposits under tree trunks and at the foot of various species of trees, especially where a dense thicket gives a protected spot. In Sierra Leone, Yorke and Blacklock found numerous pupal cases at the foot of oil-palms where the dense foliage of the lower limbs makes approach difficult. *G. morsitans* is partial to cavities in trees or stumps, or under logs or branches lying a few inches above the ground (Fig. 265). According to investigations by Lloyd, Swynnerton, and others the places for giving birth to the larvæ are not selected primarily from the standpoint of the suitability of the place for pupation of the offspring, but from the more selfish standpoint of convenience and safety for the mother. After feeding she searches a place near at hand where she can find a safe place to hide on the under surface of some object a short distance above the ground and there gives birth to her offspring, which has to make the best of the environment in which it finds itself dropped. The length of life of tsetses is probably less than a year. Specimens have been kept in the laboratory for over eight months.

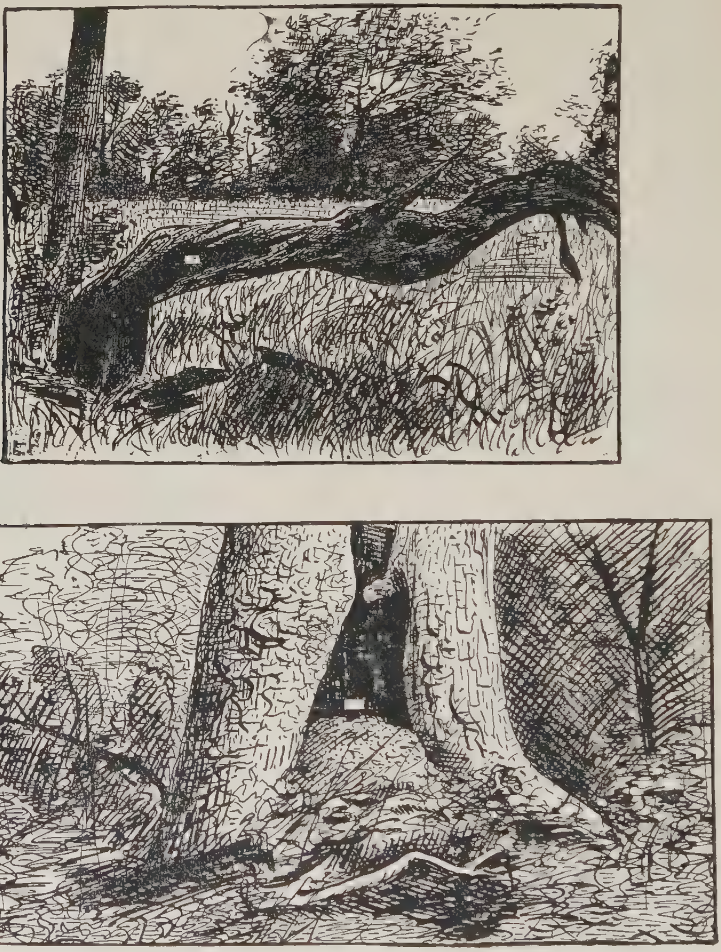


Fig. 265. Typical breeding places of *Glossina morsitans* in Rhodesia. (From photographs from Kinghorn and Yorke.)

Tsetse Flies and Disease. — As remarked before, the enormous importance of tsetse flies lies in their rôle as carriers of trypanosomes. The effect of trypanosome diseases on domestic animals in Africa has practically excluded these aids to development and civilization from some parts of that continent. The importance of trypanosomes to man in Africa is discussed in Chapter VIII. It is sufficient here to repeat that sleeping sickness, which is the final stage of trypanosome disease, is one of the most deadly diseases known.

The relation of tsetse flies to the transmission of various types of trypanosomes, particularly those of man, are discussed in Chapter VIII. Of the two trypanosomes which infect man in Africa, and are the cause of sleeping sickness, one, *Trypanosoma gambiense*, is widely distributed in West Central Africa east to Uganda and the Great Lakes; its principal transmitter is *Glossina palpalis*, but *G. tachinoides* can also transmit it, and in Northern Nigeria and Northern Cameroons has been shown to be the primary transmitter. The other trypanosome which infects man in Africa is *T. rhodesiense*, which is probably only a variety of the much more wide-spread *T. brucei;* it occurs in parts of East Africa from Tanganyika Territory to Northern Rhodesia and is transmitted mainly by *Glossina morsitans*, although in Tanganyika the closely related, darker-colored *G. swynnertoni* has been shown by Swynnerton (1923) to be the probable transmitter. It attacks man more readily than any other species.

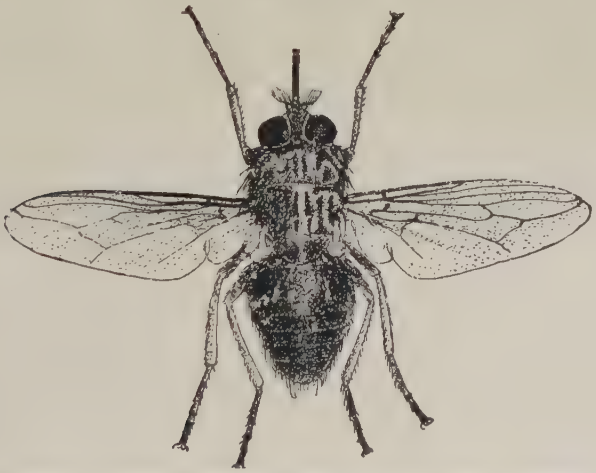


FIG. 266. *Glossina palpalis*, carrier of Gambian and Nigerian sleeping sickness. × 4. (After Austen.)

Glossina palpalis (Fig. 266) is a large dark species with blackish brown abdomen and with gray thorax having indistinct brown markings. This species is found over the whole of West Africa, from the Senegal River to Angola, and east to the upper valley of the Nile and the eastern shores of the central lakes (Fig. 261, ▧). Its range is thus nearly coincident with that of Gambian sleeping sickness. This species, more than any other except possibly *G. tachinoides,* which occurs around the southern border of the Sahara Desert, is dependent on the presence of water. Its natural range is said seldom to exceed 30 yards from the edge of water, and the distance that it will follow animals or man is not more than a few hundred yards. Muddy, reedy sloughs or swamps are not frequented by this fly, but rather sandy- or gravelly-banked streams with abundant overhanging vegetation. In the rainy season the flies extend their range to headwaters which are dry during the remainder of the year and retreat again with the drying up of the water. It is feared that this species may sometime bridge the short gape between the headwaters of the Congo and the Zambesi, and become established along the latter river and its tributaries, carrying sleeping sickness with it.

It is strictly limited to forest areas in which trees or shrubs with permanent foliage predominate, and is found neither in deep impenetrable forests or in grass lands. Since the flies always live within a few feet of the ground they demand shrubbery or thickets in which to hide. They feed on game animals to a much smaller extent than many other species, and more frequently bite such mammals as man, monkeys and dogs, and derive a large part of their sustenance from reptiles. According to Fiske the crocodile is the host of first choice, *Varanus,* a lizard, second, and the Situtunga antelope third. Goats are remarkably unattractive to the flies. It is undoubtedly the concentration of the food animals near water courses, and of suitable hiding and breeding places near them, which attract the flies to such localities rather than the water itself.

Glossina tachinoides is one of the smallest tsetse flies, being about the size of a housefly. It has very distinct bands on the abdomen, and is browner and darker than *G. morsitans.* It is found around the southern edges of the Sahara Desert and in southwestern Arabia. Its habitats are practically the same as those of *G. palpalis,* but it is satisfied with thickets more sparsely shaded by mixtures of deciduous and evergreen trees, and can withstand higher temperatures. It is seldom found near villages, but rather in sparsely settled areas where game and river animals are abundant. Its food habits are similar to those of *G. palpalis,* except that it perhaps feeds a little more frequently on mammals.

Glossina morsitans (Fig. 267), carrier of many trypanosome diseases of animals and of the lately arisen and still rather limited Rhodesian sleeping sickness, is the most widely distributed species of tsetse fly, occurring all the way across Africa from Senegal to southern Sudan and Abyssinia on the north, to northeastern Transvaal and Zululand on the south (Fig. 261, ▨). This is also the best known species, and is the one which has attracted to itself the attention of big-game hunters in Africa for many years. It is slightly smaller than *G. palpalis* and much lighter colored, with very inconspicuous markings on the gray thorax, and with more or less distinct dark bands, not continuous across the middle line, on the buff colored abdomen. As remarked elsewhere, *G. morsitans* is not confined to the immediate vicinity of water, but prefers hot dry savannahs with bush or scattered trees. In some places it is found at an altitude of over 5000 feet, but usually occurs at much lower levels. It feeds on the blood of almost any large mammal which comes its way. It was long supposed that the fly was especially dependent on the Cape buffalo, *Bubalis caffer*, as it undoubtedly was before this animal was almost exterminated by rinderpest, but the fly is certainly able to exist in the absence of the buffalo, though often in less numbers than when the abundant food supply was at hand. This species is, however, primarily a big game feeder, and normally seldom feeds on anything but mammalian blood Baboons are said to be relished by the fly in some parts of Africa. Wild and domestic pigs are often fed upon.

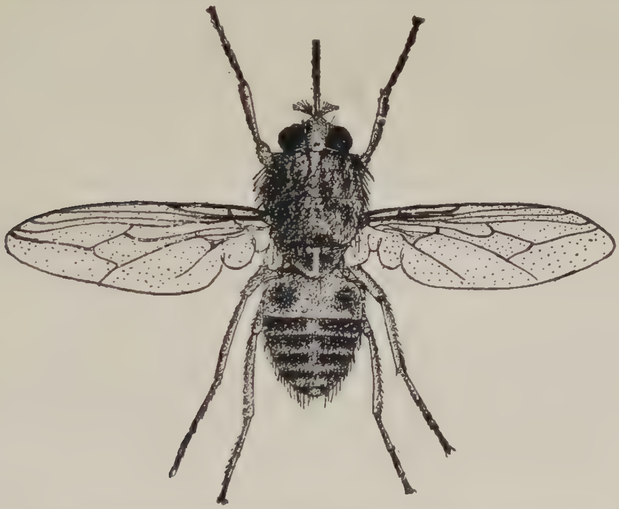


FIG. 267. *Glossina morsitans*, carrier of Rhodesian sleeping sickness. × 4. (After Austen.)

Glossina morsitans, though most active in the morning and late afternoon, sometimes bites at midday and even after dark, especially on warm moonlight nights. The habit of following moving objects is especially marked in this species, and some observers state that flies have followed them several miles, frequently alighting on the ground to rest, or on the person pursued, often without attempting to bite. The reproduction and choice of breeding places of this species have already been mentioned.

G. swynnertoni is also a dry-area fly, and has habits closely similar to those of *morsitans*, but is much more limited in its distribution.

Although *G. palpalis* and *tachinoides* are undoubtedly the normal transmitters of Gambian sleeping sickness and *G. morsitans* and *swynnertoni* of Rhodesian sleeping sickness, they are not the only species which have been found capable of transmitting these diseases, at least under laboratory conditions. *G. morsitans* has been found to be able to nurse *Trypanosoma gambiense* in some districts but not in others. *G. pallidipes*, which resembles *G. morsitans* but is larger, and confined to southeastern Africa, can be experimentally infected also.

Another species experimentally able to transmit human trypanosomes, *T. gambiense*, is *G. brevipalpis*, of South Central and East Africa. This is a large species found in abundant shade, in bush mixed with creepers and young trees near water courses. Its counterpart in the more northern parts of East Africa is *Glossina longipennis*, a large warm-brown species with indistinct markings. *G. brevipalpis* is said to be desirous of feeding only before 8.00 A.M. and after 4.00 P.M. In the middle of the day it hides under leaves or grass blades near the ground, so that its presence would never be suspected.

To sum up it may be said that while there is much variation in the susceptibility of different species of tsetses to different trypanosome infections, so that one or a few species come to serve as the usual transmitters of any particular trypanosome, yet other species cannot be definitely excluded as carriers without extended experimentation and observation. Even in the case of natural carriers of a particular trypanosome, a very small per cent of flies are found naturally infected, and not more than a few per cent can be infected experimentally. Moreover it is evident that a single species of fly shows marked differences in receptivity to infection in different parts of the range. The refractory nature of some West African races of *G. palpalis* possibly accounts for the absence of sleeping sickness in Dahomey and neighboring states. It is probable that climatic conditions and food habits play a leading part in determining susceptibility of flies to trypanosome infections.

Control. — Attacks of tsetse flies can be avoided to some extent by the use of the usual insect repellents (see p. 581), by fly-proof clothing or veils, and by wearing white clothes. When it is necessary to travel through fly-infested places where sleeping sickness occurs, all of such measures should be adopted, or, better still, the fly-belts should be passed through in the darkness of night when the insects are inactive. Railroad trains and steamboats passing through fly-belts should be protected by fly-proof screens; this expedient is adopted in many parts of Africa at the present time.

Extermination of tsetses on a large scale is a very difficult matter, but locally it is quite feasible. There are probably factors influencing the distribution of the flies which are still unknown, and which may be turned to account in destroying them.

Clearing away of brush along fly-infested streams in the case of such species as *G. palpalis* and *G. tachinoides*, which are closely confined to patches of brush along water courses, is the most valuable measure in connection with their local destruction. As said before, these flies seldom go over 50 yards from such brushy borders of streams except when following prey, in which case they may go several hundred yards. If brush is cleared away and low branches of trees cut out for a distance of 30 yards from the edge of water in the vicinity of fords, villages, washing places, etc., the flies quickly disappear, and do not reappear as long as the cleared area is *kept* clear. The effectiveness of this method of extermination has been demonstrated especially well by the Portuguese Sleeping Sickness Commission on the Island of Principe where tsetse flies were almost, though not entirely, exterminated in a four years' campaign. In addition to clearing margins of bodies of water, the beds of the water courses were straightened and leveled to make the clearing easier, and forests were completely cleared away on a large scale where they seemed to harbor tsetses. In addition some of the men employed in these operations wore on their backs black cloths smeared with sticky bird-lime, thus being converted into active traps for capturing flies. Nearly half a million flies were thus caught, and the number caught daily gave a good index to the effectiveness of the preventive measures being used, and must of itself have been a supplementary means of destruction which was of value. The effectiveness of clearing away brush and thickets has also been demonstrated in Nigeria. Grass burning is sometimes resorted to, but this impoverishes the soil and is only advocated under exceptional conditions. The eradication of *Glossina morsitans* is a much more difficult problem, since its habitats, though sharply confined to "belts," are not so closely limited to the edge of water, and are therefore more difficult to clear. Since, however, the areas occupied are usually not over a few square miles at the most, complete deforestation of such areas when near villages or highways would often be feasible.

The destruction of pupæ of tsetse flies by natural enemies undoubtedly aids in limiting their numbers. The newly deposited larvæ are covered by a slimy secretion which apparently protects them against the attacks of the ants which almost always abound in the tsetse breeding places. The pupæ are attacked by parasitic insects (Fig. 268), but apparently not to a sufficient extent to seriously reduce their numbers. It is possible that some of these insects could be successfully exploited. The adults of *G. morsitans* are attacked, according to Lamborn, by a species of dragon-fly, *Orthetrum chrysostigma*, which persistently pursues them and diligently searches the vicinity of men and animals for them.

Constructive measures should follow the destructive ones, such measures, for instance, as the cultivation of unfavorable plants and encouragement of natural enemies such as the black drongo, *Dicrurus ater*, and the small bee eater, *Melittophagus meridionalis*, which are known to feed on the adult flies.

The question of the control of tsetse flies by the wholesale destruction of wild game is a subject over which there has been much flowing of ink. The extent to which such destruction, even if possible, would actually control the flies is questionable. Lloyd carried out experiments in Nigeria by fencing off a large area to exclude game animals and studying the effect on the tsetse flies. There was a falling off in numbers of all species of tsetses, and an indication that destruction of game would ultimately exterminate *G. morsitans*, but *G. palpalis* and *tachinoides*, though reduced in numbers, showed no evidence of starvation. Tsetses do tend to disappear with the encroachment of civilization, as has been demonstrated near Elizabethville. In East Africa, on the other hand, there is good reason to believe that the appearance of Rhodesian sleeping sickness was the direct result of more frequent association of tsetses with domestic animals and man as the result of the reduction in wild game. It seems at least possible that wholesale destruction of large wild mammals, so that the flies could not move to other localities in pursuit of them, would result in the development of races of flies adapted to feeding on domestic animals and breeding under conditions existing where domestic animals are kept. The destruction of the rich and varied, and indeed unique, wild life of Africa is a measure so radical, so contrary to our present growing determination to save the irreplaceable handiworks of nature, and, to be sure, so inhuman, that it cannot be advocated or even tolerated until absolutely proved to be an effective, and the *only* effective measure.

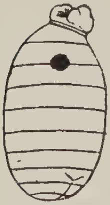


Fig. 268. Pupal case of *Glossina morsitans*, showing hole of emergence of a small chalcid parasite. × 4. (After Waterston.)

Stable-Flies (*Stomoxys*) and Their Allies

Belonging to the family Muscidæ, in company with the houseflies and tsetse flies, are a number of other biting flies, most important of which are the stable-flies, *Stomoxys*, especially the common species, *S. calci-*

trans (Fig. 269), which makes itself annoying and often dangerous in nearly every part of the world. It is chiefly a persecutor of domestic animals, but is very willing to attack man when opportunity is offered.

The stable-fly in general appearance so closely resembles the housefly, *Musca domestica*, as often to be mistaken for it, whence the frequent statement that houseflies sometimes bite. They differ, however, in several ways. The stable-fly is more robust, browner in color, rests with the wings spread at a broader angle, and has a narrow, pointed shining-black proboscis (Fig. 270) which is quite different from the blunt fleshy proboscis of the housefly.

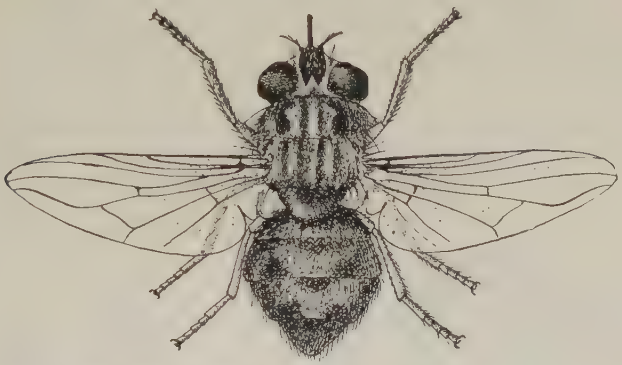


FIG. 269. Stable-fly, *Stomoxys calcitrans*. × 5.

The mouthparts (Fig. 270) differ from those of many other biting flies in that the lower lip, which usually merely forms a sheath for the piercing mouthparts, is itself a piercing organ. It is bent at nearly right angles under the head so that it projects straight forward, being, therefore, fixed to the head like a bayonet to a rifle. The short basal segment is movable and muscular, and is used to manipulate the proboscis itself. The latter has at its tip rasplike spines which aid in perforating the skin of the host. Inside the groove in the lower lip is the labrum and hypopharynx which together form a sucking tube. The maxillary palpi, which form enclosing sheaths for the proboscis in tsetse flies, are less than half the length of the proboscis in *Stomoxys*.

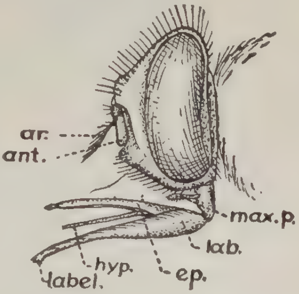


FIG. 270. Head and mouthparts of stable-fly, *Stomoxys calcitrans; ant.*, antenna; *ar.*, arista of antenna; *ep.*, epipharynx; *hyp.*, hypopharynx; *lab.*, labium; *label.*, labellum; *max. p.*, maxillary palpus. (After Herms.)

The stable-fly is commonly believed to breed in manure, and gains its name from the frequency with which it is found about stables, presumably having been bred in manure. As a matter of fact, the presence of stable-flies about stables is due to the presence there of animals — horses, cattle, etc., — on which they feed. The breeding place which is most preferred is moist, decaying straw or rotting vegetable matter. According to Herms, the very best breeding places are afforded by the left-over hay, alfalfa or grain in the bottoms of, or underneath, out-of-door feed troughs in connection with dairies. In this soggy, fermented material practically pure cultures of *Stomoxys* larvæ may be obtained.

The eggs of *Stomoxys* (Fig. 271) are banana-shaped white objects about one mm. in length, curved on one side and flat on the other, with a groove on the flat side. They are deposited, sometimes deep in the decaying material selected, in small batches of from two to half a dozen, until from 25 to 50 or more are laid; there are a number of such depositions made by a single fly during her life. The eggs hatch in from two to five days, usually three, into whitish, almost transparent footless maggots (Fig. 272*A*) very similar to those of the housefly, but easily distinguishable by the position of the posterior stigmal plates (see Fig. 295). The larvæ mature in a minimum of from 10 days to over two months, usually in about 15 to 20 days, and crawl into drier portions of the breeding material to pupate. The pupæ (Fig. 272*B*) are olive-shaped, chestnut-colored objects, 6 to 7 mm. in length. With favorable temperatures the adult fly emerges in a few days, but this period may be much prolonged by cold weather. The shortest time in which a stable-fly may develop from the time of egg-laying is about two weeks, and this

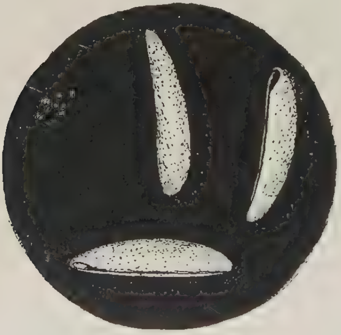


FIG. 271. Eggs of stable-fly, *Stomoxys calcitrans*. × 20. Note eggs natural size in upper corner. (After Newstead.)

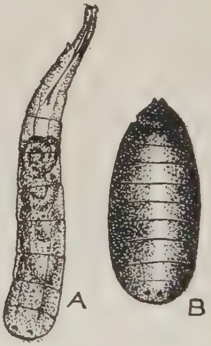


FIG. 272. Larva (*A*) and pupa (*B*) of stable-fly, *Stomoxys calcitrans*. × 4. (After Newstead.)

is extended under conditions which are not ideal. According to Herms' experiments, the average length of life of stable-flies is about 20 days. They sometimes live several months, however.

There are several other genera and species of the family Muscidæ which sometimes bite man, but none of them are habitual feeders on human blood, and they are hardly worthy of special consideration. They all resemble *Stomoxys* in general appearance, though some, notably the common hornfly, *Hæmatobia* (or *Lyperosia*) *irritans*, are much smaller. Their life histories are in general like that of *Stomoxys*, though there is some variation as regards choice of breeding places. Manure of various kinds is selected by some species, as it is by the housefly, much more than in the case of the stable-flies.

***Stomoxys* and Disease.** — Like the tabanids, the stable-flies are intermittent feeders, *i.e.*, they frequently leave one animal in the course of a meal if disturbed, to finish feeding on another. For this reason they are of importance in mechanically transmitting blood diseases.

It has been shown that the trypanosome of sleeping sickness, *T. gambiense*, can be transmitted by interrupted feeding, and a few years ago Macfie showed that the Nigerian strain of the parasite could go through at least part of its development in the gut of the black stable-fly, *Stomoxys nigra.* A number of trypanosomes of animals are mechanically transmitted by *Stomoxys.*

More serious than this is the relation of stable-flies to anthrax (see p. 529). This fatal disease of domestic animals and man is caused by bacteria which live long enough on or in the proboscis of stable-flies to be readily transmitted by them within an hour or two after an infective feed. The biting flies of this or other species which congregate to feed on sick or dying animals must be looked upon as a serious source of danger. Other diseases, such as foot-and-mouth disease, to which both animals and man are susceptible, may presumably be transmitted in like manner by these flies, though no proof of it has yet appeared.

In 1912 and 1913 several American workers, among them Dr. M. J. Rosenau, of the U. S. Public Health Service, adduced the theory that the stable-fly, *Stomoxys calcitrans*, was responsible for the transmission of infantile paralysis, and the theory was apparently supported by some facts in the epidemiology of the disease (though contradicted by others), and by carefully conducted experiments. In subsequent experiments, however, by the same and other workers, the results have been uniformly negative, and in the meantime much data has been collected to show that this terrible disease is transmitted by contagion, and *not* through the agency of any particular insects. It cannot be said that the disease is never transmitted by biting flies, or by ordinary houseflies, but that insects are not the main or even important factors in the spread of the disease is now a fairly well-established fact.

Stomoxys is still further involved in the case of animals, since it acts as the intermediate host of a parasitic worm of horses, *Habronema microstoma*, and also as the intermediate host of some of the tapeworms of chickens, which are infected by devouring the maggots.

Control. — Control of the stable-flies and of allied species of biting flies depends almost entirely on the elimination of their favorite breeding places. In the case of *Stomoxys*, which is the most important of this group of biting flies, preventive measures are fairly easy. The drying out, burning, or burying of waste vegetable matter, such as piles of weeds, wet hay, lawn clippings, waste vegetable matter in garbage heaps, etc., eliminate the main breeding places. Poorly constructed hay stacks, around which there is a good deal of loose hay which becomes soggy and decays, are breeding centers for the flies. Stacks, when needed, should be constructed with evenly rounded top and vertical sides; but a better way, when possible, is to bale hay or straw and store it in dry places. Manure especially when mixed with straw is utilized by stable-flies in lieu of better breeding places, but the principal manure-breeder is the housefly, *Musca domestica*. According to recent work by the U. S. Department of Agriculture, manure can be treated in such a way as to destroy the young stages of stable-flies and houseflies without injuring its fertilizing value. A mixture of ten oz. of borax and 12 oz. of crude calcium borate (colemanite) is applied to ten cubic feet (eight bushels) of manure, the manure being then sprinkled with two or three gallons of water. A still better substance to apply is hellebore powder, one-half lb. in ten gallons of water to eight bushels of manure. An excessive quantity of the powder has no injurious action on the fertilizing power of the manure, as has an excess of borax.

CHAPTER XXVII

MOSQUITOES

Importance. — Of all existing insect pests mosquitoes are the greatest enemies of mankind. The mere annoyance which the enormous numbers of them cause by their constant attacks and painful bites is sufficient to have made some parts of the world practically uninhabitable. There are rich pieces of country which have remained absolutely unsettled on account of this pest alone. Some of the choicest hunting and camping grounds in North America, and in other continents also, are practically closed to the camper by the countless millions of mosquitoes which transform a camper's paradise into an intolerable hell, and drive any bold human invader to frenzy. When travel through such places is necessary no comfort can be hoped for without the presence of a dense smudge or without almost constant application of "mosquito dope," and even then the unceasing "*zangs*" of the mosquitoes as they threateningly approach is hardly less trying on the nerves than are the actual attacks. Unlike most insect pests the mosquitoes of cold northern countries are if anything more abundant than they are in the tropics. The far northern mosquitoes do not, however, act as carriers of disease; terrible as they are, they wage clean warfare, whereas many tropical mosquitoes have their spears poisoned with death-dealing disease germs. The northern mosquitoes bite, suck their fill of blood if they can, and are through; the tropical mosquitoes often leave months or years of suffering and disease, or even death, in their wake. No less than four different diseases are normally transmitted by mosquitoes exclusively, namely, malaria, yellow fever, dengue or breakbone fever and filariasis, while a fifth, a form of myiasis in South America, is usually transmitted by mosquitoes. Mosquitoes have been suspected of complicity in the transmission of still other diseases, but their relation to the first four diseases mentioned above is sufficient to brand them as the greatest insect enemies of the human race.

General Structure. — Mosquitoes, which constitute the family Culicidæ, belong to the large order Diptera, the general characteristics and classification of which have been considered in the preceding chapter. They belong to the Nemocera division of the suborder Orthorrhapha (see p. 505), the same division to which belong the sandflies, blackflies, and midges (Chironomidæ), and numerous non-blood-sucking forms such as crane flies, gall gnats, etc., many of which are important agricultural pests. The Culicidæ can easily be distinguished from all other Diptera, some of which superficially resemble them, by the presence of scales along the wing veins, and a conspicuous fringe of scales along the hind margin of the wings. Most of the Culicidæ have a long prominent proboscis containing needle-like organs for piercing and sucking, but in one subfamily, including the so-called phantom midges, *Corethra*, the adults of which resemble true mosquitoes and are often mistaken for them, there is no long proboscis.

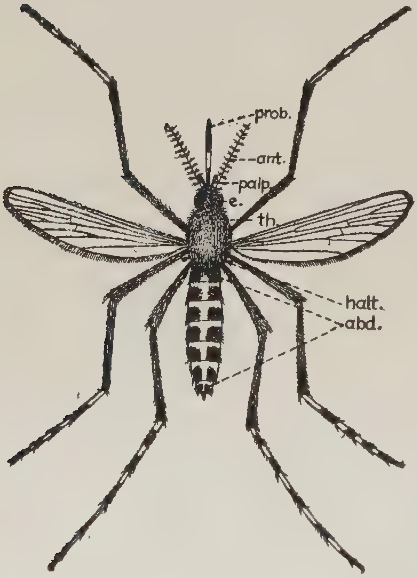


Fig. 273. Diagram of adult female mosquito (*Aëdes sollicitans*); *abd.*, abdomen; *ant.*, antenna; *e.*, eye; *halt.*, haltere; *palp.*, palpus; *prob.*, proboscis; *th.*, thorax.

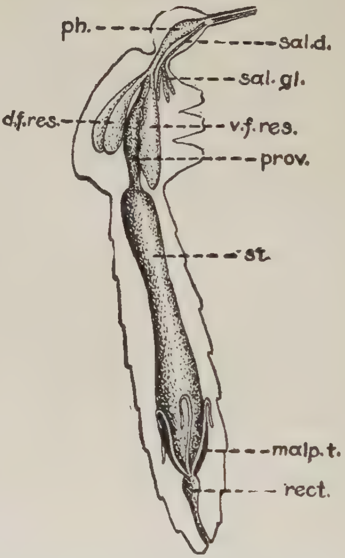


Fig. 274. Digestive tract of a mosquito; *d. f. res.*, dorsal food reservoirs; *malp. t.*, malpighian tubules; *ph.*, pharynx; *prov.*, proventriculus; *rect.*, rectum; *sal. d.*, salivary duct; *sal. gl.*, salivary gland; *st.*, stomach; *v. f. res.*, ventral food reservoir.

The general appearance of adult mosquitoes is so well known as to need no description, but the details of their structure is as little known by most people as are those of the structure of other insects. Figures 273, 274 and 170 illustrate the main features of a mosquito. The sexes can be distinguished most readily by the antennæ; in the female (Fig. 275*A*) they are long and slender with a whorl of short hairs at each joint, whereas in the male (Fig. 275*B*) they are shortened and have a feathery appearance, due to tufts of long and numerous hairs at the joints. In many mosquitoes the palpi also furnish a means of distinguishing the sexes; they are usually long in the males but short in the females, but in *Anopheles* they are long in both sexes, and in some mosquitoes, *e.g. Uranotænia*, they are short in both.

The proboscis, which is the most fearful part of a mosquito, also differs in the sexes, and fortunately is so constructed in the male that a mosquito of this sex could not pierce flesh if he would. At first glance the proboscis appears to be a simple bristle, sometimes curved, but when dissected and examined with a microscope it is found to consist of a number of needle-like organs lying in a groove in the fleshy lower lip, which was the only part visible before dissection. In the female mosquito there are six of these needle-like organs, the nature and names of which are shown in Fig. 276. The " labrum-epipharynx " and " hypopharynx " act together to form a tube for drawing up blood into the mouth. A tiny tube runs down through the hypopharynx, opening at its tip, through which saliva is poured into the wound as through a hypodermic needle to prevent blood from coagulating. The ensheathing lower lip does not itself penetrate the wound, but bows back as the mosquito bites, the flexible tip or " labellum " acting as a guide for the piercing organs as they are sunk into the flesh. In male mosquitoes the piercing organs are much degenerated, only the suctorial part of the apparatus being well developed.

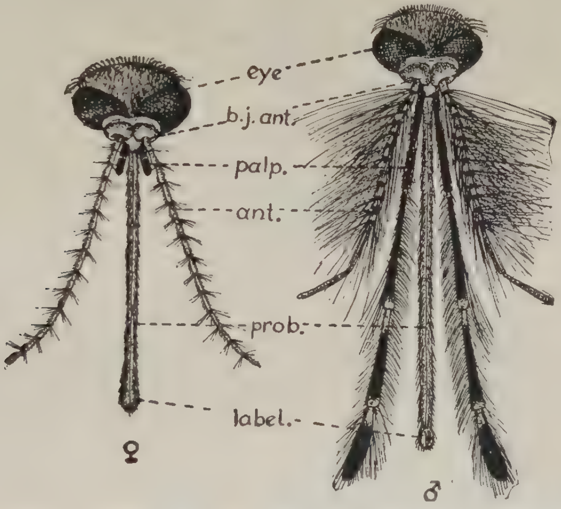


FIG. 275. Heads of female (♀) and male (♂) mosquito, *Culicella incidens; ant.*, antenna; *b. j. ant.*, basal joint of antenna; *label.*, labellum; *palp.*, palpus; *prob.*, proboscis.

Besides the variations of the parts mentioned already, adult mosquitoes vary as regards the form, distribution, color and other characteristics of the scales which clothe much of the body and the edges and veins of the wings; the details of the male reproductive organs at the tip of the abdomen (hypopygium), the details of which in a representative *Culex* and *Anopheles* are shown in Fig. 277; the details of the female hypopygium; the relative length of parts of the leg; and in other respects.

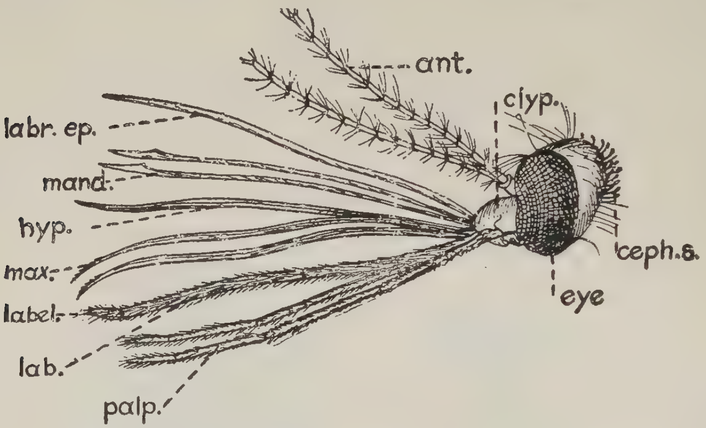


FIG. 276. Side view of head of female *Anopheles* showing mouthparts; *ant.*, antennæ; *clyp.*, clypeus; *ceph.*, *s.* cephalic scales; *hyp.*, hypopharynx; *lab.*, labium; *label.*, labellum; *labr. ep.*, labrum-epipharynx; *mand.*, mandibles; *max.*, maxillæ; *palp.*, maxillary palpi. × 20. (After Nuttall and Shipley.)

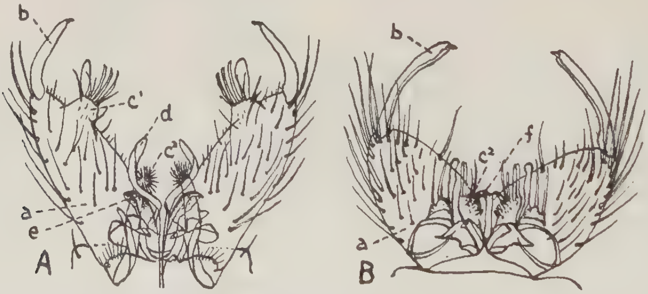


FIG. 277. Male genitalia of mosquitoes; *A*, *Culex quinquefasciatus*, *B*, *Anopheles quadrimaculatus;* *a*, side piece; *b*, clasper filament; c^1, upper lobe of side piece; c^2, lower lobe of side piece; *d*, harpago; *e*, harpe; *f.*, uncus. (After Howard, Dyar and Knab.)

All mosquitoes have good " capacity " as far as the digestive tract is concerned, having three food reservoirs connected with the esophagus, in addition to a large stomach (Fig. 274). Recent investigations indicate that these reservoirs are used for storage of " aspirated " foods, such as fruit juices, but not for blood, the latter passing directly to the stomach. This practically precludes the possibility of *direct* transmission of disease germs immediately after an infective feed. Connected with the proboscis is a pair of salivary glands consisting of three lobes each. One of these lobes in each gland differs from the others and instead of secreting ordinary saliva is thought to secrete the poisonous substance which prevents coagulation of blood and produces the inflammation and pain attendant upon a mosquito bite. Schaudinn, however, has adduced some experimental evidence that it is the contents of food reservoirs which cause the inflammation. It is in the salivary glands that the malaria parasites, and probably the parasites of dengue and yellow fever also, collect, and whence they are poured with the secretions of the glands into the wounds.

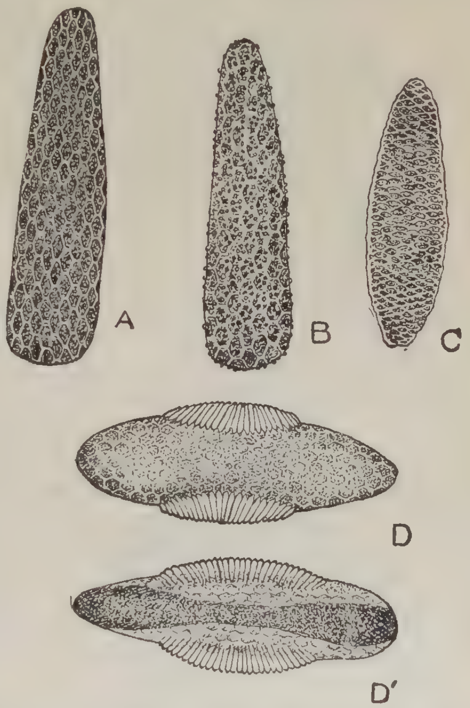


FIG. 278. Eggs of mosquitoes; *A*, *Culicella inornatus;* *B*, *Mansonia perturbans;* *C*, *Aëdes ægypti;* *D*, *Anopheles punctipennis*, dorsal view; *D′*, same, ventral view. × 75. (After Howard, Dyar and Knab.)

Life History. — Mosquitoes, like other Diptera, pass through a complete metamorphosis in the course of their life history, *i.e.*, they undergo a transformation from larval to adult stages during a period of rest. In a general way the life histories of all mosquitoes are much alike, but in details there is much variation among them. Without special adaptations in habits and physiology to meet the exigencies of their diverse environments there would be little chance for the mosquitoes of the frozen north or of the parched tropical deserts to meet successfully the struggle for existence. A great store of interesting facts concerning the life history and habits of mosquitoes has been collected by Howard, Dyar and Knab in Part I of their " Monograph of the Mosquitoes of North and Central America and the West Indies " and much of the information incorporated into this chapter has been taken from their work.

The eggs of mosquitoes (Fig. 278) are usually oval, with various surface markings, and in *Anopheles* with a peculiar " float " of air cells. The number of eggs laid by a single female mosquito varies from 40 or 50 to several hundred. Some species lay their eggs singly (Fig. 279) while others lay them all at one time in little boat-shaped rafts called egg-boats, the individual eggs standing upright (Fig. 280). The fact that the eggs are a little larger at the lower end makes the whole egg-boat slightly concave, thus making it difficult to overturn. Most of the common mosquitoes of temperate climates lay their eggs on the open surface of water or attach them to some partially submerged object; a few species lay eggs which sink. Many species, however, especially those of the far north and of the tropics, lay their eggs in dry places which are likely subsequently to be covered with water. In most mosquitoes of temperate climates the eggs hatch in a few days, or even within 24 hours. In the species of the far north the eggs probably never hatch until the following spring, being laid in depressions on the ground which are usually not immersed until the melting of the winter snows. Such hibernating eggs are said not to hatch unless they have been exposed to freezing temperatures. On the other hand the mosquitoes of dry hot countries lay eggs which are highly resistant to desiccation and do not lose their vitality during months of dryness. Such species must almost " live while the rain falls," and to win in the struggle against an unfavorable climate they must be prepared to utilize the most transitory pools for the completion of their aquatic immature stages. In such cases the embryo within the egg shell develops to the hatching point, so that it is ready to begin the larval existence almost with the first drop of rain. Such mosquitoes further fortify their race against the unkind environment by laying their eggs in a number of small batches instead of in a single mass, as is the habit with mosquitoes where water is plentiful. Just as a man runs less risk of ruin if he deposits his money in a number

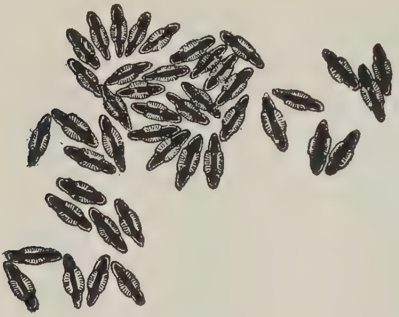


FIG. 279. Eggs of *Anopheles quadrimaculatus* on surface of water. × 13. (After Howard.)

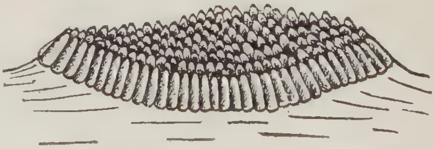


FIG. 280. Egg boat of *Culex* floating on water. × about 8.

of insecure banks rather than in a single uncertain one, so it is with mosquitoes and the places where they deposit their eggs. The gamble for life in a dry climate would be too risky if all eggs were deposited in one place, and species with this habit have probably long since been weeded out in the struggle for existence. Another remarkable adaptation of dry-climate mosquitoes is the variation in the hatching periods of the eggs in the same batch; not all hatch with the first drops of moisture, but some lie over until subsequent immersions, thus insuring a much better chance that some of them, at least, will not waste their life on the desert air with too little water to enable them to reach maturity.

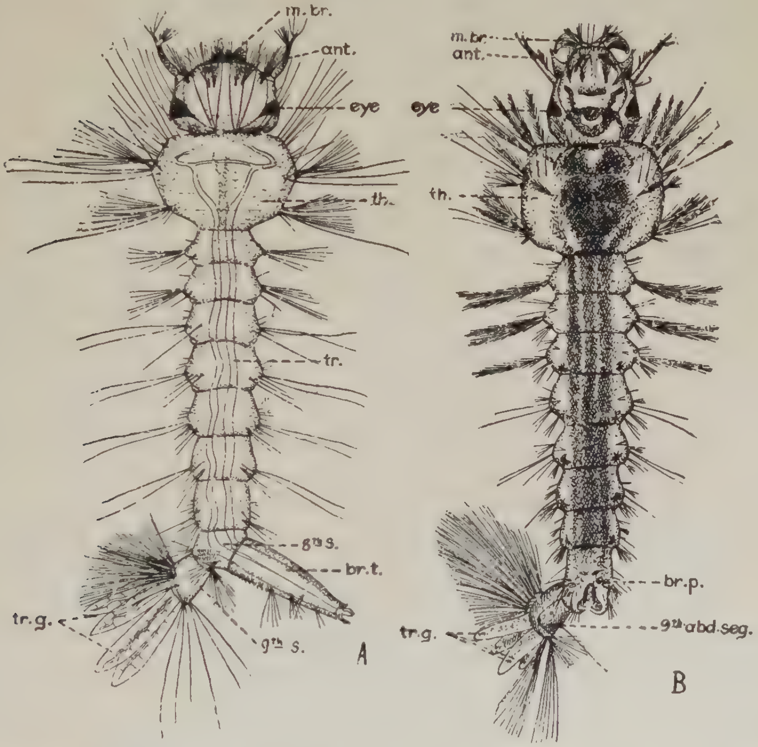


Fig. 281. *A*, Larva of tropical house mosquito, *Culex quinquefasciatus; ant.*, antennæ; *br. t.*, breathing tube or siphon; *m. br.*, mouth brushes; *th.*, thorax; *8th s.*, 8th abdominal segment; *9th s.*, 9th abdominal segment; *tr.*, tracheæ; *tr. g.*, tracheal gills. *B*, Larva of *Anopheles punctipennis;* note absence of breathing tube, and starlike groups of scales on abdominal segments; *m. br.*, mouth brushes; *br. p.*, breathing pore; other abbrev. as on Fig. *A*. × 10. (After Howard, Dyar and Knab.)

The eggs of mosquitoes never hatch except in the presence of water. The larvæ, which are always aquatic, are very active wormlike creatures, well known as " wrigglers " or " wiggle-tails " (Fig. 281). When first hatched they are almost microscopic, but they grow rapidly to a length of from 8 to 15 or 20 mm. The bunches of long bristly hairs on the body take the place of legs, and aid the larva in maintaining a position in the water. The "rotary mouth brush" is a brush of stiff hairs which is used to sweep small objects toward the mouth; in predaceous species these are sometimes modified into rakelike structures or into strong hooked bristles for holding prey. The trumpet-shaped breathing tube (Fig. 281*A*) is present on all mosquito larvæ except *Anopheles* (Fig. 281*B*), in which it is undeveloped. It is used to pierce the surface film of the water to draw air into the air tubes or tracheæ inside the body, for, although aquatic, mosquito larvæ are air breathers, and make frequent trips to the surface to replenish their air supply, remaining suspended by the breathing tube from the surface of the water while breathing. The leaflike "tracheal gills" on the last segment of the abdomen differ from true gills in that air tubes or tracheæ instead of blood-vessels ramify in them. In one genus of mosquitos, *Mansonia*, the larvæ absorb air from the air-carrying tissues in the roots of certain aquatic plants, piercing them with the apex of the breathing tube and thus avoiding the necessity of rising to the surface of the water. In well-aërated water the larvæ can live without surface air for a long time by using their tracheal gills, but they die within a few hours if shut in water without dissolved air.

Mosquito larvæ, unless suspended from the surface film by means of the breathing tube, have a tendency to sink and they rise again only by an active jerking of the abdomen, using it as a sculling organ. Some species are habitual bottom feeders, others feed at the surface; some live on microscopic organisms, others on dead organic matter, and still others attack and devour other aquatic animals, including young mosquito larvæ of their own and other species.

The larvæ shed their skins four times and then go into the resting pupal stage. Mosquitoes of temperate climates usually take from five days to two weeks to complete the larval existence, depending almost entirely on temperature and abundance of food. In the mosquitoes adapted to take advantage of transitory rain-pools the larvæ may transform into pupæ within two days and the pupal stage is a mere matter of hours. On the other hand, some mosquitoes habitually pass the winter as larvæ.

While the larvæ of anopheles are easily distinguished from those of other mosquitoes by the absence of a breathing tube, the identification of larvæ within these groups is more difficult. Anopheles larvæ are especially difficult to distinguish, their differentiation depending on very minute differences in the form and arrangement of particular bristles.

The larvæ of culicines are usually more easily identified by the nature of the tuft of hairs on the antennæ, the relative length and breadth of the breathing tube, the number of tufts of hairs on the breathing tube, the number and arrangement of the scales in the scale patch on the eighth segment, presence of single or multiple head hairs, etc.

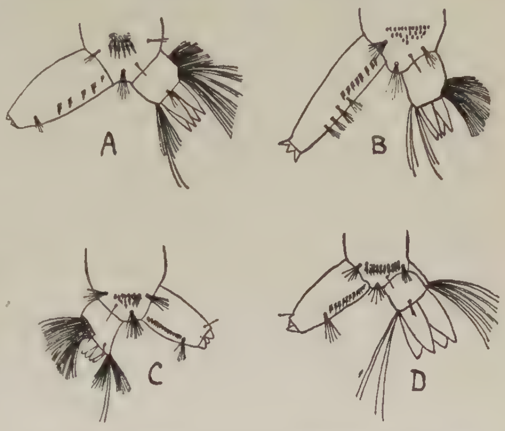


Fig. 282. Posterior ends of representative mosquito larvæ; *A*, *Psorophora columbiæ; B*, *Culex quinquefasciatus; C*, *Aëdes sollicitans; D*, *Aëdes ægypti.* (After Komp.)

The general form of the pupa can be seen in Fig. 283. Alcock has aptly described this stage of a mosquito as resembling a tiny lobster deprived of appendages and carrying its tail bent. The pair of earlike breathing tubes on the cephalothorax (head and thorax fused) take the place of the trumpet-like tube of the larva and are used in the same manner. Unlike the larva the pupa is lighter than water, and requires muscular effort to sink instead of to rise.

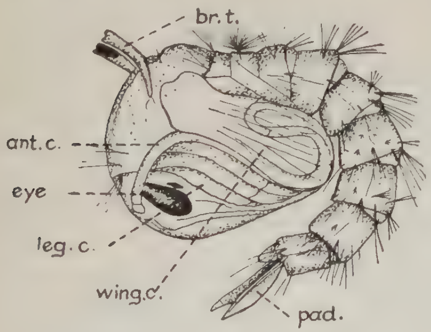


Fig. 283. Pupa of house mosquito, *Culex pipiens; ant. c.*, antennal case; *br. t.*, breathing tubes; *leg. c.*, leg cases; *pad.*, paddles; *wing c.*, wing case. × 10. (After Howard, Dyar and Knab.)

As remarked before, the transformation into the adult during the pupal stage may be a matter of a few hours in the case of the dry-climate mosquitoes, but in most species it requires from two days to a week, depending on the temperature. The adult mosquito emerges head first through a longitudinal slit along the back of the thorax. After its exit it rests for a moment on the old pupa skin, stretches and dries its wings, and then takes flight.

Habits of Adults. — Adult mosquitoes vary to a remarkable degree as regards habitats, feeding habits, mode of hibernation, choice of breeding grounds, and other habits. The knowledge that each species of mosquito has habits and habitats more or less peculiar to itself is of great economic importance, since it does away with useless expenditure in combating harmless or relatively harmless species, and aids in the fight against particularly noxious ones. The fact, for instance, that one of the commonest summer mosquitoes of northeastern United States, *Culex territans*, does not annoy man does away with the necessity of destroying larvæ in certain kinds of marshes and pools where this is practically the only breeder. Again, the fact that mosquitoes breeding in crab holes do not annoy man eliminates the necessity of attempting the almost impossible task of destroying such breeding grounds in order to be free of mosquitoes. The fact that a certain species of *Anopheles*, *A. eiseni*, which is a tree-hole breeder, is not a malaria carrier, saved thousands of dollars in the anti-malarial fight in the Canal Zone.

Habitats. — A classification of mosquitoes according to habitats and breeding grounds has been attempted by some authors. Dr. J. B. Smith, for instance, divides the mosquitoes of New Jersey into four ecologic groups, the salt marsh, house, swamp, and woodland mosquitoes. However, almost as many different ecologic groups could be made as there are species of mosquitoes or possible breeding and foraging places. There are species which breed in reedy swamps, woodland pools, eddies of rivers, slow-flowing streams, holes in trees, pools of melted snow, salt marshes, tide pools, crab holes, pitcher plants and other water-bearing plants, or in broken bamboo stems filled with water. There are species which have become " domesticated " and occur almost always in the vicinity of houses, laying their eggs in water troughs, street gutters, rain barrels, water-filled cans in garbage heaps, flower vases, water bottles, coconut shells, and any other collection of water in or about human habitations. Some species show almost no preference as regards breeding places, others, especially those breeding in such specialized places as in water-holding plants, are very closely limited; some species prefer pure clear water, others filthy water, while still others are apparently indifferent.

Much work has recently been done, especially by Senior-White, on the factors which determine whether or not mosquitoes will breed in certain bodies of water. Different species of mosquitoes come and go through the seasons in regular succession; each species selects a definite type of habitat and is often associated with definite types of plant growth; and often in waters which look superficially similar certain mosquitoes will breed in one and not in another. Attempts have been made to correlate these peculiarities with acidity or alkalinity, oxygen concentration, density of dissolved solids, particular forms of algæ which might serve as food, etc. Nearly all of this work has been fruitless since mosquitoes show a wide tolerance to all of these factors individually. With respect to the concentration of saline ammonia alone has a definite correlation with the breeding of certain species been demonstrated; a concentration of more than 1 part per million was found to be injurious to all the Indian species of *Anopheles* tested except the innocuous *A. rossi*. It is suggested that increase of nitrogen in soil by leguminous plants or manuring may act as an inhibiting factor on malaria-carrying mosquitoes, providing the activity of such nitrifying bacteria as *Nitrosomonas* could be controlled, perhaps by a bacteriophage. The complexity of the problem is great, for odors may attract or repel the females searching for places to lay eggs; substances in the water may be directly injurious to the larvæ; or, what is probably usually the dominant factor, the quantity or quality of the food may or may not be suitable. Most mosquito larvæ, however, have been shown to be able to use a considerable variety of foods, though usually living organisms are preferred. Barber has successfully reared certain larvæ on algæ, bacteria or ciliates alone. The associations in water are fundamental; in the reasons which underlie these is hidden everything that has any bearing on the biology of each species; they are the product of the interaction of all the physical and chemical processes present. Biological control of mosquitoes may eventually be possible, but so far only the surface has been scratched. Watson says " Drainage schemes may become things of the past and future generations may smile to think how their ancestors, who thought they were so clever, burned the house to cook the pig."

Migration. — That mosquitoes are seldom found far from their breeding grounds is another fact, only recently recognized, of great economic importance. Most kinds of mosquitoes seldom stray more than from half a mile to a mile from their birthplace, and many not over a few hundred yards. The supposition that mosquitoes utilize a strong wind to carry them long distances is entirely false, since mosquitoes are so delicate as to be unable to fly at all with a strong wind but remain hidden away at times when such wind storms occur. Some mosquitoes are able to resist moderate winds, but nearly always fly *against* them instead of with them. The salt marsh mosquitoes are an exception to the sedentary nature of mosquitoes. These mosquitoes commonly migrate for a number of miles and may go as much as 40 miles inland from the salt marshes which bred them. The common salt marsh mosquito, *Aëdes sollicitans* (Fig. 273), the mosquito that made New Jersey famous, breeds in enormous numbers in the marshes of the Atlantic and Gulf coasts of the United States, often depositing its eggs in dry mud. The advent of a heavy rain may cause the egg production of months to hatch, and literally billions of mosquitoes are simultaneously produced, which under favorable conditions of temperature, humidity and breeze migrate inland to torment the inhabitants of neighboring cities and towns. Such towns are subject to occasional sudden invasions of clouds of mosquitoes which, however, seldom stay more than a few days at any great distance from the marshes. With the exception of a few of these salt marsh species, an abundance of mosquitoes can almost always be looked upon as evidence of the existence of breeding places near at hand; I have been repeatedly impressed with the fact that when mosquitoes are seriously complained of in cities, I have seldom failed to find a breeding place within a block, and often in the immediate vicinity of the house whence the complaint came.

Although most species are not migratory, railroad trains, street cars, ships and other conveyances are efficient means of transfer for mosquitoes. Hawaii is said to have been free of these pests until they were introduced with sailing vessels, in which mosquitoes can usually find plenty of water for breeding. The great number of trains daily running inland in New Jersey from the marsh-studded coast is undoubtedly a factor in keeping more distant suburban towns stocked. Well established cases are on record of places once free of mosquitoes becoming infested after the advent of railroad or boat service.

Time of Activity. — Although mosquitoes are usually looked upon as strictly nocturnal, and though this is true of most of the common species of temperate climates, it is by no means characteristic of the whole group. Many species, including most *Anopheles*, are active chiefly at twilight in the evening or early morning. Knab found that the mosquitoes of northern prairies, where the nights are too cold for them, are active throughout the day only. A large proportion of forest-living tropical species, at least in America, are said to be diurnal. Some of the mosquitoes of the northern woods are apparently ready to bite when a victim approaches, whether it be day or night. The widely distributed yellow fever mosquito, *Aëdes ægypti* (or *Stegomyia fasciata*) (Fig. 287), feeds by preference in the early morning or late afternoon. Here again a knowledge of the habits of particular species is of importance, since it may aid in the intelligent avoidance of particular disease-carrying forms.

Food Habits. — Heretical as it may sound, mosquitoes feed mainly on plant juices, honey, etc. It is doubtful if the males of *any* species normally suck blood, and even the females of some species are strict vegetarians. On the other hand, the females of many species have a voracious craving for warm blood and cannot produce eggs without it. Some species indiscriminately attack any warm-blooded or even cold-blooded animal, while others show strong preferences. The yellow fever mosquito normally feeds chiefly on man, and even discriminates against the black race. The other " domestic " mosquitoes apparently have a strong liking for human blood also, and it is not unlikely that their domestic habits are the result of their taste for human blood. Knab found that *Aëdes spenceri* of the Saskatchewan prairies would fly toward any large object. On the prairies such an object would usually be a large animal and the mosquitoes would fly towards it instinctively in the hope of satiating the craving for food.

Hibernation. — The method employed by mosquitoes for passing the winter in cold climates, and the dry season in the tropics, varies with the species. Many of the mosquitoes of temperate climates and many in the tropics hibernate or pass the dry season in the adult stage, the females stowing themselves away in hollows in trees, caves, crevices in rocks, cellars, barns, etc., to come forth and lay their eggs in the spring. A few species hibernate in the larval stage, the larvæ of one species, *Wyeomyia smithii*, becoming enclosed in solid ice in the leaves of the pitcher plant in which they live. Most hibernating larvæ retire to the bottom of their breeding pools during cold weather and do not survive freezing. Many temperate- and warm-climate mosquitoes and all of the northern ones pass the unfavorable season in the egg state, and this may be looked upon as the *common* method of hibernation. Many anopheles survive the cold season either as adults or as larvæ, but usually not as eggs.

Length of Life. — The length of life of mosquitoes varies with the species and with the sex. Male mosquitoes seldom live more than from one to three weeks; their duty in life is done when they have fertilized the females. The latter usually die shortly after they have laid their eggs but some species may live for four months or more. The species which lay all their eggs in a mass at one time are short lived, and have several generations a year, whereas those in which the eggs are laid in small lots, at intervals, live for several months. Species in which the females hibernate are still longer lived, but since they are not active in winter their *effective* life is short.

Classification. — Over 500 species of mosquitoes have been described, the majority of which belong in the tropics, although the north is richer in individuals. The task of classifying all of these species into subfamilies and genera is one which has taxed the wits of many scientists. The wide discrepancies in the work of different men as regards mosquito classification is the best possible proof of the difficulties in the way. As in many other groups of animals, intensive study has tended to magnify the value of certain characteristics as criteria of genera or subfamilies, the result being the breaking up of what would ordinarily be looked upon as a single group into a number of poorly defined and intergrading groups. Theobald, who has written a monograph of the mosquitoes of the world, separates the Corethrinæ (forms without a long proboscis) from the mosquitoes, and divides the remainder of the family into ten subfamilies and a very large number of genera based largely on scale characteristics. On the other hand, Howard, Dyar and Knab, whose classification is adopted here, recognize only two subfamilies — the Corethrinæ and the Culicinæ, the latter including all the true mosquitoes. The Culicinæ are further divided into two tribes, the Sabethini, including chiefly forest-dwelling non-blood-sucking forms, and the Culicini. The genera of the latter are arranged in a series from the primitive forms of the genus *Anopheles* to such highly specialized forms as *Megarhinus.* Later Dyar divided the Culicinæ into five tribes, three of which, the Anophelini, Uranotæniini and Megarhini, have only one genus each, while the Sabethini and Culicini have several. Some of the genera, including *Anopheles*, *Aëdes* and *Culex*, have been divided into subgenera, but there is considerable difference of opinion about the validity and limits of these, and they are therefore not considered here, with the exception of the subgenus *Stegomyia* of the genus *Aëdes*, which forms such a well defined group from the standpoint of habits and color, as well as disease transmission, that it is here used for convenience.

The identification of species of mosquitoes, or even of genera, is often very difficult for anyone but a specialist. Fortunately some of the most important disease-carrying species are so marked that they can quite readily be distinguished even by a novice. Only a few of the disease-bearing species can be separately described here.

Mosquitoes and Malaria

As was shown in Chapter IX, malaria is one of the most important and one of the most deadly of human diseases. This being true, the mosquitoes, which are the sole means of transmitting the disease, must be looked upon as among the most important and most deadly enemies of the human race. The rôle of mosquitoes in causing disease, especially malaria, has been suspected by various peoples as far back as any records go. The steps which led to the *proof* of the relation of mosquitoes to malaria are briefly outlined on p. 160.

Fortunately not all mosquitoes are malaria carriers; in fact, only one genus, *Anopheles*, comprising a number of more or less well-defined subgenera which have been considered genera by some workers, is known to be able to transmit the human malarial diseases, and not even all of the species of this genus are incriminated. The majority of the species can be experimentally infected with malaria parasites, but some much more readily than others, and there also appears to be a difference in the facility with which certain species can be infected with each of the three species of malaria parasites. The malaria parasites of birds are transmitted, primarily at least, by certain species of *Culex*.

As has been repeatedly pointed out elsewhere, mere experimental infection of an insect with a disease germ, or even its successful transmission under experimental conditions, means very little with respect to its rôle in nature. Many other factors come into play which cannot possibly be studied in the laboratory, and the combined effect of which can only be learned by extensive and carefully studied epidemiological evidence. Excellent examples of proved malaria transmitters in the laboratory, which are of almost no significance in nature, are *Anopheles punctipennis* of the United States and *A. rossi* of India. These insects owe their relative harmlessness to entirely difference reasons. *A. punctipennis* is eliminated by its habits; it is a " wild " species which seldom enters occupied houses, although it sometimes bites on porches or out-houses; it has a very distinct food preference for cattle and other large domestic animals and shows a distinct aversion to human blood. *A. rossi*, on the other hand, is a very common, widespread, and essentially domestic mosquito, very commonly found in houses and readily biting the human inhabitants, but in nature it only rarely becomes infected with malaria parasites. There is no epidemiological evidence whatever that either of these species is ever involved in any serious outbreaks of malaria, or that malaria continues to exist in localities in which only these species are present. Similar situations exist with respect to many other species of *Anopheles*. It is, therefore, necessary that the habits, food preferences, facility in nursing the malaria parasites, and perhaps other factors be taken into consideration in determining the dangerousness of a species as a malaria carrier. Furthermore, a mosquito which is an effective transmitter in one locality may be ineffective in another, due to availability of other hosts from which it can suck blood, or situation of breeding places with respect to human habitations. There has even been suggested the possibility of hereditary physiological races which prefer man or animals as food. Thus in Europe Roubaud has developed the theory that the immunity of certain localities in France to malaria in spite of the presence of the most important European transmitter, *A. maculipennis*, is due to the fact that cattle are kept under the same roof with the peasants and serve as buffers. The la Vendée marshes are said to be probably more densely populated with anopheles than any other region in the world, yet malaria is disappearing. Roubaud's belief in the development of a race of anopheles which rejects human blood for that of animals has not been confirmed in America; more likely the condition is due to the conditions under which the animals are kept. A damp dark cow-shed between a human habitation and an anopheles breeding place may afford almost complete protection. Legendre, however, introduced *Culex pipiens* from Brittany, where this species shows a repugnance to human blood, to Pons, where it feeds habitually on man, and in the following year observed a similar repugnance of this species at Pons. Much valuable information on food preferences of anopheles has been obtained by precipitin tests of the blood obtained from their stomachs, a method which we have seen yielded valuable results in the case of *Phlebotomus* also. King and Bull tested the three common anopheles of southeastern United States, only one of which, *A. quadrimaculatus*, is known to be an important carrier in nature, with the following results:

Species	No. ex'd.	per cent fed on man	cattle	pigs	horses	dogs	birds
A. quadrimaculatus....	272	32.4	48.1	15.1	2.5	1.5	.8
A. crucians...........	236	1.3	66.5	14.1	12.8	4.2	.9
A. punctipennis.......	10	all on animals					

Of 652 *A. pseudopunctipennis*, the principal malaria transmitter in Northern Argentina, Davis found that 50% had fed on man, 21.8% on dogs, and only 23% on all the large domestic animals combined.

The rôle of the mosquito in the spread of malaria and the development of the parasites in the mosquito's body have been discussed in Chapter IX, pp. 165–167. Suffice it to repeat here that the sexual phase of the life history of all malaria parasites occurs in the digestive tract of mosquitoes, after which a rapid multiplication of the germs takes place, resulting ultimately in the collection of large numbers of the parasites in the salivary glands of the insect, whence they are poured into the capillaries in the skin of the subsequent victims of the mosquito.

Identification of Anopheles. — The anopheles mosquitoes, fortunately, are fairly easy to identify in all stages of their development except as pupæ. They represent a primitive group of mosquitoes, and in many respects are less specialized than other members of the family. The different species of the genus vary a great deal as regards choice of breeding places, habits and appearance, so that it is necessary in any malarial district to determine, if possible, which species are malaria carriers, how they may be identified, where they breed, and what their habits are. The majority of the species have mottled or spotted wings, and the arrangement of the markings is usually a good means of identification (Fig. 284).

The following comparative table (Fig. 285) shows in a graphic way how *Anopheles* may ordinarily be distinguished from other common mosquitoes, such as *Culex*, *Aëdes*, etc., in their different stages. The "floats" on the eggs of anopheles are rarely absent; their size and markings sometimes serve as means of identification of species. Due to the effects of surface tension the eggs of anopheles tend to assume geometrical patterns on the surface of the water. The larvæ, besides the absence of a breathing tube and their horizontal floating position at the surface of the water, have other characteristic features such as the rosette-like "palmate hairs" on some of the segments, which serve to hold the larvæ in the characteristic position by surface tension. The species of anopheles larvæ are very difficult to identify, and reliance must be placed on the form, number and distribution of characteristic hairs; Root has published a key to the full-grown anopheles larvæ of America. The pupæ are indistinguishable as yet; even a differentiation between anopheles and culicine pupæ is uncertain. The adults are usually easily distinguishable by the resting position, with the proboscis, thorax and abdomen all in a straight line and at an angle to the resting surface, in contrast to the parallel abdomen and hump-backed appearance of culicines, but some of them, *e.g. A. culicifacies* of India, resemble the culicines in resting position. *A. quadrimaculatus* is much more culicine-like than are other North American anopheles; it rests at only a slight angle to the surface, whereas *punctipennis* appears almost to stand on its head. Most anopheles have the wings marked with dark or light spots or both, but even this is not constant, since a few culicines have spotted wings and a few anopheles, *e.g. A. atropos*, have unspotted ones. The long palpi of the females is a character which can always be relied upon.

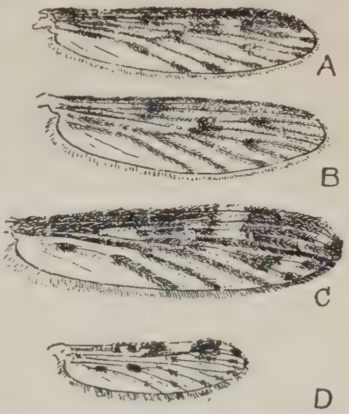


FIG. 284. Wings of American *Anopheles; A, A. crucians; B, A. quadrimaculatus; C, A. punctipennis; D, A. albimanus.* Drawn to scale. (After Howard, Dyar and Knab.)

Habits of Anopheles. — Most anopheles are breeders in natural waters such as ponds, swamps, edges of streams, rice fields, grassy ditches, etc. Few species breed in artificial containers, *A. stephensi* of India being a prominent exception; it breeds in such containers as cisterns

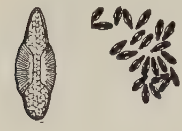
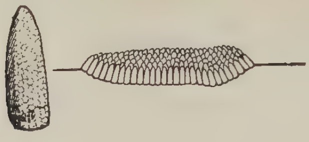
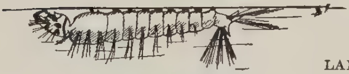
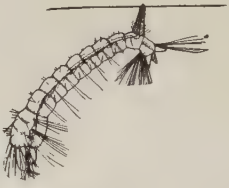
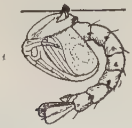
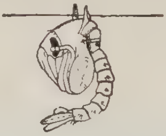
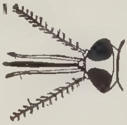
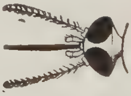
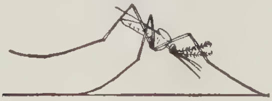
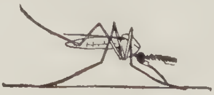
	Anopheles	*Culex, Aëdes,* etc.
EGGS	 Eggs laid singly on surface of water; provided with a partial envelope, more or less inflated, acting as a "float."	 Eggs laid in rafts or egg-boats, or singly on or near water, or where water may accumulate; never provided with a "float."
LARVÆ	 Larvæ have no long breathing tube or siphon; rest just under surface of water and lie parallel with it.	 Larvæ have distinct breathing tube or siphon on 8th segment of abdomen; hang from surface film by this siphon, except in *Mansonia*, which obtains air from aquatic plants.
PUPÆ	 Pupæ have short breathing trumpets; usually do not hang straight down from surface of water.	 Pupæ have breathing trumpets of various length; often hang nearly straight down from surface of water.
HEADS OF ADULTS	 Palpi of both male and female long and jointed, equaling or exceeding the proboscis in both sexes.	 Palpi of female always much shorter than proboscis, those of male usually long, but sometimes short.
RESTING POSITION OF ADULT	 Adult rests with body more or less at angle with surface, the proboscis held in straight line with body.	 Adult usually rests with body parallel to surface, though sometimes at an angle. Proboscis not held in straight line with body, giving "hump-backed" appearance.

Fig. 285.

and wells in Indian cities. Although nearly all anopheles are natural water breeders the different species show very marked preferences. Of the American species, *A. quadrimaculatus* and *A. crucians* breed in ponds, swamps, rice fields, grassy pools, etc., where plankton is abundant, and both will tolerate rather brackish water; *A. punctipennis* prefers to breed in or near clear running water or in wells where the plankton is relatively scanty; *A. pseudopunctipennis* breeds in reservoirs, cat-tail marshes, etc., where there is abundant plankton and clean water; *A. atropos* breeds in salt marshes. Many species prefer deeply shaded jungle streams or forest swamps, *e.g.*, *A. grabhami* of tropical America, *A. funestus* of Africa, and *A. umbrosus* of southeast Asia; others choose still, alga-filled waters exposed directly to the sun, such as *A. albimanus* of tropical America, *A. gambiæ* (=*costalis*) of Africa and *A. barbirostris* of Asia. In Malaya the cutting down of jungle in the flat lands and exposure of sluggish water to sunlight changes a dominance of *umbrosus* to *barbirostris*, with a reduction in malaria; but when ravines in the hills are opened up and the sparkling streams cleared of vegetation and exposed to sunlight, the virgin jungle species, especially *A. aitkeni*, disappear and the deadly *A. maculatus* takes their place. Thus in the two localities directly opposite conditions determine the presence or absence of malaria. Some anopheles, such as *A. ludlowi*, an important malaria carrier in southeast Asia, seldom breed except in strongly brackish water, and some species are said to breed in pure or even concentrated sea-water. Some of the coral islands of the East Indies are practically uninhabitable for newcomers on account of the prevalence of malaria carried by anopheles breeding in quiet pools within the coral reefs. Other species, as *A. eiseni* of Central America, breed in tree holes; *A. cruzi* of Brazil breeds in accumulations of water in the leaves of certain tropical plants.

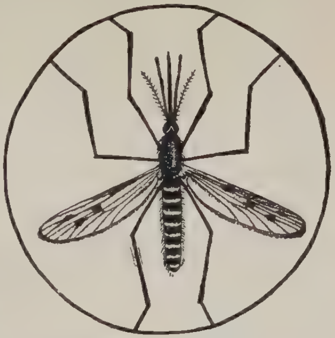


FIG. 286. The common North American malarial mosquito, *Anopheles quadrimaculatus*.

It is important to note that while the various species of anopheles show strong preferences in their breeding places, and can generally be controlled by an attack on such places, exceptions abound. The breeding places in some localities may be quite different from those in others, and often places which appear to be ideal breeding places are avoided, due to some local combination of chemical, physical or biological characteristics which affect either the larvæ or their food or enemies.

The eggs of anopheles are not as resistant to drying as are those of *Aëdes*, but will survive for as long as three weeks on drying mud, and even the larvæ can live on moist mud for some time. The eggs hatch only in water, and at temperatures above 60° C.; under favorable conditions they hatch in from 1 to 2 days. The larvæ are chiefly surface feeders; they seem to feed on any particles floating on or near the surface which is small enough to swallow but thrive best on floating algæ, particularly diatoms. Anopheles larvæ are not rapid in their development as compared with some mosquitoes, the time required under favorable conditions being from two to three weeks or more, — from 1 to 3 days for the eggs, usually from 10 to 20 or more for the larvæ and from 2 to 7 for the pupæ. The number of generations a year probably varies greatly with the species and conditions of food and temperature. It has been estimated that *A. quadrimaculatus* has from 8 to 10 annual generations in southeastern United States.

Adult anopheles are for the most part twilight feeders, and do not suck food either in broad daylight or in the darkness of night, but there are many exceptions to this. Some species are known to come forth at different times in the evening, some with the first shade of late afternoon, others not until almost dark. According to Roubaud *A. maculipennis* in France is active mainly from 12 to 2 at night, while a few species, *e.g.*, *A. braziliensis*, are diurnal; many forest species will bite willingly in the daytime if disturbed. The food preferences of adult females and its important bearing on malaria transmission has already been discussed. Another important observation made by Roubaud is that the adults, at least of *A. maculipennis*, fly out into the open and invade other houses or sheds even if there is an abundant food supply where they have been resting after an earlier meal; as a result the anopheles population of any spot is entirely changed in a few days; this flight in the open seems to be indispensable to the life of *A. maculipennis*, and it, too, has an important bearing on malaria transmission. Mosquitoes do not suck blood daily; usually blood meals are taken at intervals of several days.

Most anopheles are rather sedentary in habit, and seldom fly in numbers more than a fraction of a mile from their breeding places; *A. quadrimaculatus* is more of a traveller than most species, but even it rarely goes more than 1½ miles from its breeding place. As a rule, when anopheles are abundant a breeding place can be found within a half-mile.

Many anopheles hibernate either as adults or as larvæ, and frequently in both ways, but usually not as eggs. Hibernating larvæ bury themselves in mud or under débris at the bottom of water where they remain quiescent, only coming to the surface momentarily when disturbed. When the temperature rises they come to the surface to feed.

Malaria-Carrying Species. — Over a hundred species of *Anopheles* have been described and they occur all over the temperate and tropical parts of the world. Although not more than about half of these species have been proved to be able to harbor malarial parasites and nurse them to the weaning point, the number of incriminated species is constantly growing, and it is the safest plan to look upon any anopheles as a potential malaria carrier until proved otherwise. Often the habits of the species, as already shown, is of more importance than the ability to transmit the disease under experimental conditions. The difference in ability of some species of anopheles to nurse one type of malaria more readily than another still further complicates the task of evaluating the rôle of different species. *A. quadrimaculatus*, for instance, seems to be a more effective transmitter of tertian and quartan than of the more deadly malignant tertian malaria.

In most countries experience has shown that although numerous species of anopheles may exist, there are usually only a few species which are associated with extensive malaria. In North America *A. quadrimaculatus* is primarily involved, with *A. crucians* serving as an occasional transmitter, and perhaps involved in small local outbreaks, whereas *A. punctipennis* alone is never associated with extensive malaria. In Central America and the West Indies *A. albimanus* is principally involved; in Brazil and northern South America it is *A. argyritarsus* and *A. tarsimaculatus;* in Northern Argentina and the Andes, *A. pseudopunctipennis;* in Europe, *A. maculipennis;* in Africa, *A. gambiæ* (=*costalis*) and *A. funestus;* in India, *A. listoni*, *culicifacies*, *funestus*, *stephensi* and others; in Malaya *A. umbrosus* and *A. maculatus;* in the East Indies *A. ludlowi;* in Japan and probably parts of China, *A. hyrcanus* var. *sinensis*, and in Formosa *A. minimus;* in Australia, *A. annulipes*. These species undoubtedly account for the majority of all the malaria in the world, but many other species also contribute and may be locally the prime factors.

The effect of anti-anopheles campaigns on the prevalence of malaria is discussed in Chapter IX, pp. 177–179.

Mosquitoes and Yellow Fever

Following upon the heels of the discovery of the relation of mosquitoes to malaria, and second only to it in importance, came the discovery of a similar relation to yellow fever, in 1900. As in the case of malaria, some physicians suspected the instrumentality of mosquitoes in the dissemination of this disease before there was any proof of it. The proof came as the result of the illustrious work of the American Army Yellow Fever Commission, composed of Doctors Reed, Carroll, Lazear, and Agramonte, at the cost, indirectly, of the lives of three of them. What is known of the nature of yellow fever, and of the rôle of the mosquito in transmitting it, is discussed in Chapter X, pp. 194–196. The organism which causes the disease is still in doubt, for while Noguchi, whose life also was sacrificed to the study of this dread disease, adduced very weighty evidence in favor of the causation of yellow fever by a spirochæte, *Leptospira icteroides*, doubt has been cast on the correctness of his deductions, which are no longer accepted. The blood of a yellow fever patient can infect a mosquito only during the first few days of illness, and the mosquito cannot usually transmit the disease in less than 12 days later, although the minimum may be $8\frac{1}{2}$ to 10 days. In one case, hereditary transmission of yellow fever from an infected mosquito to its offspring has been stated to occur.

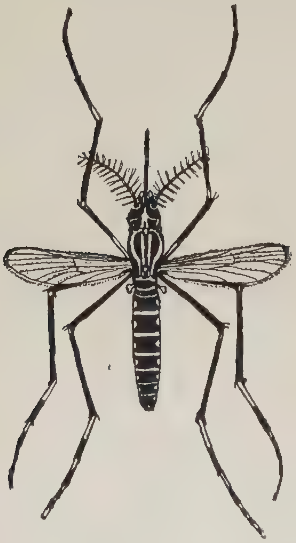


Fig. 287. Yellow fever mosquito, *Aëdes calopus*, female. (After Doane.)

The Transmitting Species, *Aëdes ægypti*. — The most important transmitter of yellow fever in nature is *Aëdes ægypti* (alias *A. argenteus*, *A. calopus* and *Stegomyia fasciata*), and until recently it was the only species known to be involved. A number of other American species have been experimented with, with negative results, but Bauer (1928) and Philip (1929) have found that some other West African mosquitoes can transmit the disease to monkeys. These include the very common *Aëdes vittatus* (=*sugens*) which has habits similar to *A. ægypti*, and *A. luteocephalus*, *A. apicoannulatus*, *A. africanus*, *A. simpsoni*, and a species of a related genus, *Eretmopodites chrysogaster*, most of which are tree-hole breeders.

Aëdes ægypti, the yellow fever mosquito, has been known in medical literature as *Stegomyia fasciata* for so long, and the subgenus *Stegomyia* is so well marked in its habits and coloration, that it seems desirable to use the name " stegomyia " as a common name. It is a small black species, conspicuously marked by silvery-white bands on the legs and abdomen, and a white lyre-shaped design on the thorax. The female, which, of course, is the only sex connected with the transmission of disease, since the males do not suck blood, has very short palpi which are white at the tip. The wings are clear and somewhat iridescent.

Habits of *Aëdes ægypti.* — The yellow fever mosquito is the most thoroughly " domesticated " species known. It is seldom found except in the vicinity of houses and shows a decided preference for human blood. As a rule it seldom leaves the rooms of houses except to find a suitable place to lay its eggs. Long familiarity with man has made this mosquito one of the most elusive and well-adapted pests of the human race which nature has ever evolved. Its stealthy attack from behind; its habit of crawling up under the clothing to bite in preference to attacking the exposed ankles; the suppression of the characteristic mosquito "song," so that its bite comes silently and without warning; its habit of concealing itself in pockets, folds, etc., of garments; its hiding behind pictures, under chairs, etc.; the wariness of its larvæ; — all these are the result of lessons learned from long and close association with man.

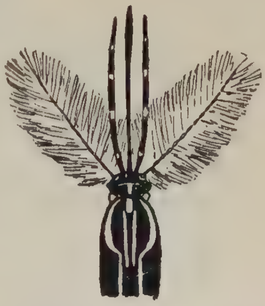


FIG. 288. Head of *Aëdes ægypti*, male. (After Goldberger.)

Aëdes ægypti is principally a diurnal mosquito, and becomes particularly hungry in the early morning and during the afternoon. While it appears to bite by preference in daylight, experiments show that it will also bite at night, especially if deprived of an opportunity to feed in the day. The conclusion of the French Yellow Fever Commission that the yellow fever mosquito bites only at night after the first week or so of its life, and also the conclusions of others that no biting occurs at night, are equally erroneous. The observation that danger of infection is greater for persons sleeping in an infected locality, than for visitors during the daytime only, is probably due to the fact that most of the mosquitoes obtain a meal early in the morning or towards evening.

Breeding. — *Aëdes ægypti* never lays eggs until it has had a meal of blood and when water or moist surfaces are available. According to recent experiments by Bacot a single male mosquito may fertilize a number of females. Fertile eggs are usually laid a few days after a blood meal. The mosquitoes commonly feed every 4 or 5 days, but do not lay eggs after each meal; in captivity females have been observed to lay up to 750 eggs over a period of 72 days. All of the stegomyias seem to be partial to artificial containers as breeding places, especially *A. ægypti*, although they probably come from a race of tree-hole breeders; some of the stegomyias still revert to this habit when tree holes are close to human habitations. *A. œgypti* much prefers rain barrels, wooden water butts, water-filled tin cans in garbage heaps, coconut shells, sagging roof gutters, flooded cement floors in cellars, jardinieres and flower vases, toilet tanks, and, in fact, almost any manner of container other than ground pools. Churches in Central America are usually well supplied with yellow fever mosquitoes which breed in the holy water fonts unless sponges are substituted for the open water. The statement that they do not breed in iron containers is not entirely true; I have found them in abundance in iron barrels used for storing water for fire protection. When complaints of local abundance of this mosquito are heard, it is best to look first for a breeding place in or immediately around the house, next in the yard or compound, and never further than the yards or compounds within a city block.

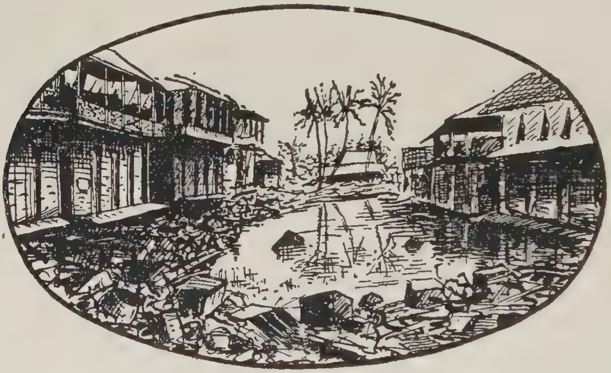


Fig. 289. A yellow fever center in Panama in the pre-American days. (Drawn from photo from Thompson.)

The eggs (Fig. 278*C*) are laid in batches of about 30 to 50 at a time at intervals of several days, either on the surface of water or, more commonly, on the sides of the container or of projecting objects where a moist surface is presented and where a slight elevation of water will submerge them. I have frequently found drinking-water barrels infected with newly hatched larvæ immediately after being filled with fresh water, the owners naturally complaining that the delivered water contained the larvæ The eggs are capable of retaining their vitality when dried for 8 or 9 months after a preliminary incubation in water or on a wet surface. Eggs laid on the surface of water hatch in a minimum of two days, whereas eggs laid above it, if later submerged, may hatch in less than 24 hours after oviposition. Strangely enough not all the eggs hatch at once; some are refractory, and if a batch of eggs is exposed to repeated drying and submersion, the eggs hatch a few at a time, and some even at the end of five or six weeks, after 20 or more submersions. Such a condition is, of course, a great protection to a species which breeds in such precarious collections of water as does this one. Hatching can be stimulated by a lowering of temperature, or by addition of lysol, soap or sea water. Atkin and Bacot found that eggs which failed to hatch in distilled water did so a few hours after the introduction of living bacteria.

The larvæ (Fig. 290) thrive best in moderately clean water, and will not breed in very foul water such as *Culex quinquefasciatus* delights in. Atkin and Bacot have shown that the food consists almost, if not quite, exclusively of bacteria, and that when the larvæ are present in large numbers they exert a considerable influence on the purification of water. Often the larvæ are overlooked, since they immediately wriggle to the bottom of their dwelling place when approached, and hug the bottom so closely that even if a barrel containing thousands of them is turned over on its side, a high percentage will stay in the little remaining water. The larvæ feed exclusively on the bottom and can often be seen nibbling away at a dead insect or bit of decaying vegetation. With plenty of food and at favorable temperatures the larval existence may be completed in four days, according to Bacot, though it usually requires a longer time than this, and may be drawn out to two months or more. The larvæ are not resistant to drying, and die in a few hours in a dry place, though capable of living nearly two weeks on moist ground.

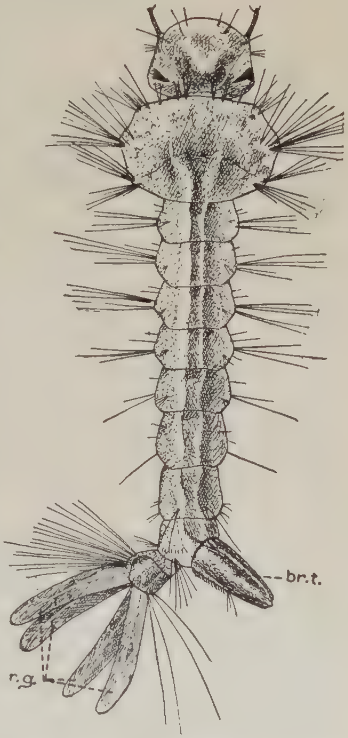


FIG. 290. Larva of yellow fever mosquito, *Aëdes ægypti*. × 10. (After Howard, Dyar and Knab.)

The pupæ (Fig. 291) transform, under normal conditions, in a day and a half or two days. The entire cycle from egg to adult seldom takes place in less than nine or ten days, and probably 12 or 15 days is more usual under ordinary conditions. As has been shown above, the period of development may be drawn out over several months by unfavorable conditions. The adult mosquitoes may live for a considerable time, and apparently are able to transmit yellow fever any time from 10 or 12 days after infection to the end of their lives. Male mosquitoes ordinarily will not live beyond 50 days, but the females frequently live under laboratory conditions for four months or more; they die shortly after the last batch of eggs has been laid. Kind of food, dryness of climate and facilities for laying eggs are among the chief factors determining the length of life of these mosquitoes, and, strange as it appears at first, the length of life is shortest under the most favorable conditions, namely, plenty of blood for food, plenty of moisture, and suitable places for egg-laying.

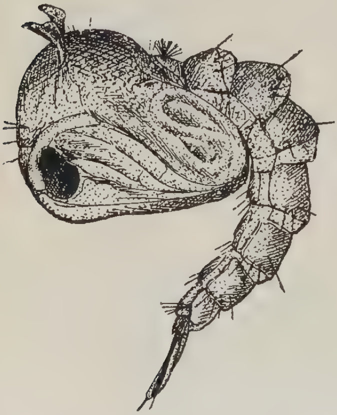


FIG. 291. Pupa of yellow fever mosquito, *Aëdes ægypti*. ×10. (After Howard, Dyar and Knab.)

The flight of the yellow fever mosquito is strong but, like most other mosquitoes, it seldom flies long distances, usually not more than a few hundred feet. Vessels lying half a mile from shore rarely if ever are visited by these mosquitoes unless the latter are carried from shore by lighters or boats.

Owing to its domestic habits and its ability to "stow away" the yellow fever mosquito has been, and annually is, widely distributed over the world. All other stegomyias are Old World species, and Dyar believes it probable that *A. ægypti* originated in the Old World also; if this is true it is probable that yellow fever is also of Old World origin, probably having been brought to America from West Africa where it is still endemic. *A. ægypti* is now a permanent resident in practically the entire warm portion of the world, wherever a temperature of 80° or more is maintained for any length of time, and where freezing does not occur. The once common occurrence and breeding of this mosquito during summer months in cities of the Atlantic Coast of the United States and in other ports outside the frostless zones was due to its importation on ships from such infested cities as New Orleans, Havana and Rio de Janeiro. The cool nights and low summer temperatures on the Pacific Coast of the United States prevents its thriving there, in spite of the fact that it is still sometimes carried there on ships. Since the great reduction of this mosquito in many of the ports where it was once abundant its importation to other places has become less frequent. Since *Aëdes ægypti* has a much wider range than has yellow fever there is constant danger of the introduction of the disease into places where it has not previously been known and where, due to the non-immune condition of the people, it would become a terrible scourge if once successfully introduced. The introduction of yellow fever into southeastern Asia or Australia by infected human beings from the present endemic areas in West Africa and America is impossible on account of the long sea voyage, but introduction of infected mosquitoes is an ever-present menace. Attempts to control the local abundance of this mosquito in non-infected lands is therefore important in order to lessen the possibility of rapid spread if such an unfortunate thing should occur.

Mosquitoes and Dengue

The relation of mosquitoes to dengue or breakbone fever was first pointed out by Graham, of Beirut, in 1902, who performed experiments which showed that this disease was not caught by close association with patients in the absence of mosquitoes, whereas isolated men subjected to bites from mosquitoes which had bitten dengue patients readily contracted the disease. Other workers adduced evidence in favor of the mosquito transmission of the disease, and Ashburn and Craig in the Philippines showed that laboratory-bred mosquitoes, fed on dengue patients, could transmit the disease three days after the infective meal. The nature of the disease and development of it in mosquitoes and man is discussed in Chapter X, pp. 196–197. It is a disease which resembles a mild form of yellow fever, is seldom fatal, and occurs in very sweeping and rapidly traveling epidemics.

Transmitting Species. — Although the earlier work of Graham (1902) and of Ashburn and Craig (1907) pointed to the tropical house mosquito, *Culex quinquefasciatus* (= *fatigans*) as the species primarily involved, all subsequent workers, including Cleland, Bradley and MacDonald in Australia, Chandler and Rice in Texas, and Siler, Hall and Hitchens in the Philippines, in more carefully controlled experiments, have failed to incriminate this mosquito but have conclusively demonstrated that, in most places at least, the yellow fever mosquito, *A. ægypti*, is the guilty species. Japanese investigators in Formosa have experimentally transmitted the disease by another stegomyia, *A. albopictus* (= *scutellaris*), and another mosquito of the *Aëdes* group, *Armigeres obturbans*, but not *Culex*. In addition to the experimental evidence there is a large amount of strong epidemiological evidence which unmistakably points to stegomyia as the usual if not the sole transmitting mosquito. In some countries there are dengue-like diseases the transmission of which is uncertain, and it is sometimes difficult to distinguish between true dengue and papataci fever, which is transmitted by a *Phlebotomus*.

According to the work of Chandler and Rice stegomyias become infected after feeding on patients in the first to fifth days of the disease, and can transmit the infection as early as 24 hours after an infective feed, but Siler *et al.* in the Philippines got different results; they found the patient to be infective for the mosquito for only three days, and for 6 to 18 hours prior to the onset, and also failed to transmit the disease in less than 11 days after a mosquito had obtained an infective feed. This incubation period was later shortened to 8 days by Schule. The only adequate explanation for these discrepant results lies in the possibility of hereditary transmission in mosquitoes, and the use by Chandler and Rice of infected stock for breeding experimental mosquitoes. The fact that papataci fever is hereditarily transmitted among sandflies makes it appear probable that this can also occur in the case of dengue and mosquitoes, in spite of some preliminary results to the contrary. The rapid spread of dengue epidemics does not fit in well with a long incubation period in mosquitoes unless hereditary transmission is possible. Once a mosquito becomes infective it appears to remain so for the rest of its life.

Mosquitoes and Filaria

The discovery by Sir Patrick Manson in 1879 of the function of the mosquito as an intermediate host of filarial worms, the larvæ of which live in the blood, marked the beginning of a new era in medical science; it was the first evidence of the development of organisms causing human disease in the bodies of insects. An account of the life cycle of filarial worms, including the development in the bodies of mosquitoes, the means by which the worms are returned to their primary hosts, and the effect of filarial infection on man, will be found in Chapter XVIII, pp. 350–357.

Wuchereria (*Filaria*) *bancrofti* is the only one of the species of filariæ attacking man which is known to be transmitted by mosquitoes, though some of the others undergo partial development, up to the " sausage " stage, in these insects. The species of the genus *Dirofilaria* which inhabit the heart and subcutaneous tissues of dogs are transmitted by mosquitoes, and this is probably true also of the *Dirofilaria*, *D. magalhãesi*, recorded once in man.

In contrast to the condition existing with respect to malaria and yellow fever, *Wuchereria bancrofti* is not limited to one group of mosquitoes for intermediate hosts, though by no means all species of mosquitoes serve equally well as transmitters. Some fail entirely, some allow only partial development to occur, and some allow only a relatively small percentage of the ingested embryos to reach the infective stage; others, on the other hand, are too hospitable, and are frequently killed by the heavy infections which develop; apparently the most critical time for the mosquitoes is during the migration of the matured larvæ from breast muscles to proboscis. Although certain species of all the main groups of mosquitoes serve as intermediate hosts, it is interesting to note that most of the successful " nurses " are the species which are particularly domestic in habits, and feed mainly on human blood. The mosquito in which development takes place most easily is *Aëdes variegatus* (= *pseudoscutellaris*) of the East Indian and South Sea Islands. A very high percentage of the ingested embryos develop successfully, — too successfully, for many of the infected mosquitoes succumb to the infections. This is a day-biting mosquito, and in those places where it functions as the principal transmitter the filarial embryos lack " periodicity " and are present in the blood by day as well as night (see p. 352). In most other parts of the world *Culex quinquefasciatus* (= *fatigans*) plays the leading rôle, although in China and Japan it is replaced by the nearly related *C. pipiens*. Other mosquitoes which are easily infected experimentally are *Aëdes togoi* in Japan, *Anopheles rossi* in India and *Anopheles gambiæ* (= *costalis*) in Africa. Successful transmission of filariæ by mosquitoes, as of plague by fleas, depends on more than mere ability of the species to allow development of the parasites; some of the cases of frequency of filarial infections in one locality and rarity in another one not far distant, with suitable transmitting mosquitoes in both places, have not been satisfactorily explained. Undoubtedly conditions of temperature and humidity are involved. Sundar Rao, in Calcutta, found a distinct seasonal variation in the percentage of infected " wild " mosquitoes (*C. quinquefasciatus*) ranging from 3% in July to 12.5% in November and December. Humidity and temperature also influence the successful transfer of larvæ to a host when a mosquito harboring them bites, as shown on p. 354.

As already remarked, *Culex quinquefasciatus*, better known in medical literature as *C. fatigans*, can be considered the most important transmitter in most places. This mosquito is brown in color, with a broad whitish band on each abdominal segment. The thorax and legs are plain brown except for a pale area at the base of the legs.

This species is very common in houses in all thickly populated parts of tropical and subtropical portions of the world, though not so thoroughly " domestic " as *Aëdes ægypti*. In America it becomes abundant in summer as far north as Washington and St. Louis. It is strictly nocturnal and will bite in complete darkness, therefore its activity supplements that of the yellow fever mosquito, the latter taking the day shift, the former the night shift. The house mosquito does not pursue man with as much devilish cunning and perseverance as does

Aëdes ægypti, and, indeed, shows a very inferior grade of intelligence as compared with it. There is reason to believe that it is primarily a persecutor of birds and poultry, and attacks man only as a second choice. *C. quinquefasciatus* breeds in almost any standing water but apparently prefers artificial receptacles and is partial to filthy water. It very commonly breeds in cesspools and open sewers. The eggs, about 200 to 300 in number, are laid in rafts as is the case with other members of the genus. The larvæ (Fig. 281*A*), which hatch in from one to three days, have long breathing tubes, and feed chiefly on microscopic organisms. The length of time required for the mosquitoes to reach the adult stage from the time the eggs are laid depends very largely on temperature, food conditions, etc. The minimum period is probably about five or six days.

Alcock remarks about this mosquito: "Apart from its practical importance, *Culex fatigans* (or *Culex quinquefasciatus*) has a peculiar interest as being the living document of two discoveries of the first magnitude in the history of medicine, namely, Sir Patrick Manson's discovery . . . of the part played by mosquitoes in the life cycle of certain filarial blood-parasites, and Sir Ronald Ross's discovery . . . of the necessary connection between mosquitoes and certain Protozoön blood-parasites. The first discovery laid open a new world to Pathology; the second, which is the outcome of the first, will affect the destiny of the human race."

Mosquitoes and *Dermatobia*

In many parts of tropical America where the man-infesting botfly, *Dermatobia hominis* (see Chapter XXVIII, pp. 594–597), is found there has long been a belief among the natives that the maggots of this fly, which develop under the skin of man and of many other animals, are in some way the result of mosquito bites. As far back as 1653 a Jesuit priest wrote as follows: "In some of the warm lowlands there is a species of mosquito . . . somewhat reddish. In each wound produced by this mosquito, soon grows within the flesh a spine-covered worm, the size of a haricot bean or even larger . . ." (quoted from Sambon). In many localities the maggot is known by the natives as a "mosquito worm." The interesting discovery by Morales in 1911 of a mosquito with 8 relatively large eggs glued to the under side of its abdomen from which *Dermatobia* larvæ developed, and similar observations by Tovar, indicated that mosquitoes served as means of transportation for the eggs of the fly. Subsequent investigations confirmed this. In 1924 Tovar placed captured *Dermatobia* with specimens of various kinds of mosquitoes, and bundles of eggs were laid by the flies on all of 15 specimens of various species of *Psorophora* but on none of the others. Other insects, he says, were sometimes seized by the flies, but were treated with violence and discarded damaged, whereas *Psorophora* were always treated gently and liberated unharmed. Both in nature and in the laboratory other Diptera, such as houseflies, woodland Muscidæ, and other large mosquitoes have been found to serve as involuntary carriers of the eggs of this fly, and Dunn believes that in Panama a tick is involved, but the large, brightly colored mosquitoes of the genus *Psorophora* appear to be the most frequent means by which *Dermatobia* arranges for her eggs to reach the skin of a host. The suggestions of Da Matta that eggs are also laid on leaves, sweaty clothing or directly on the skin of animals seem to need confirmation, according to Newstead and Potts. It is quite probable that a fly, impelled by the urgent desire to oviposit, might be content to deposit her eggs on insects which could not very well serve the purpose of transporting the eggs to a suitable host if no *Psorophora* were at hand; or if about to "plant" her eggs on a mosquito which then escaped, the eggs might be left on the nearest object. Eggs so laid produce larvæ only if kept moist, and perish if dried. There is now no question but that mosquitoes normally serve as involuntary carriers of *Dermatobia* eggs. As Rincones put it, the mosquitoes serve as aeroplanes for the transportation of the eggs to a suitable host. This is one of the strangest inter-relations of animals in the whole realm of nature, comparable perhaps with the manner in which certain mites of the family Tyroglyphidæ assume a special travelling garb and adhere to the appendages of flies to obtain transportation to new feeding grounds (see p. 404).

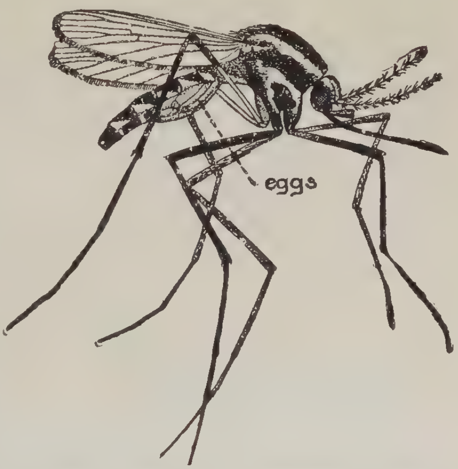


Fig. 292. *Psorophora* (*Janthinosoma*) *lutzi* with eggs of *Dermatobia hominis* attached to abdomen. (After Sambon.)

The mosquitoes involved in nature seem to be, primarily at least, species of *Psorophora*, subgenus *Janthinosoma*. In Central America *P. lutzii* alone has been incriminated, but in South America other species also, as *P. ferox* (= *posticatus*) and *P. cyanescens* (= *tovari*) also have been found to serve as hosts for the eggs. Probably any of these large mosquitoes will serve equally well. *P. lutzii* (Fig. 292) is a dark, beautifully colored mosquito, with yellow markings on the thorax, and with flashes of metallic violet and sky blue on its thorax and abdomen. It is said by Knab to be one of the most blood-thirsty of American mosquitoes and is found throughout tropical America. The larvæ breed in rain puddles, the eggs being laid in dry depressions on the forest floor which will become basins of water after a tropical downpour. The eggs hatch almost with the first drop of rain, and mature so rapidly that adult insects may emerge in 4 or 5 days. The larvæ feed on vegetable matter, and are themselves fed upon by the larvæ of the closely related mosquitoes of the subgenus *Psorophora* of the same genus, which breed in the same rainpools.

Mosquito Bites and Remedies for Them

As has been remarked before, the pain and irritation produced by a mosquito bite is usually believed to be due to the injection of a bit of poisonous saliva into the wound made by the piercing mouthparts of the insect. The susceptibility of some people to the effect of mosquito poison is much greater than that of others. I have seen individuals on whom mosquito bites swelled up like bee stings and were even more painful, whereas I myself have frequently been unaware of the fact that a mosquito was biting unless the insect was seen or was pointed out by a less indifferent companion. Moreover, the effect of the bites of different species of mosquitoes varies, so that while some species may produce very little irritation others may prove unbearably annoying. Dr. Smith, of New Jersey, became practically immune to the bites of some of the salt marsh mosquitoes, but was troubled by the house mosquito, *Culex pipiens*, and still more so by anopheles. I have had similar experiences, and have found myself driven almost to frenzy by some species and hardly annoyed at all by others. It is quite probable that the complaints which are heard from visitors to the ocean resorts of the New Jersey coast are due to the fact that these visitors are fully susceptible to the poison of the salt marsh mosquitoes whereas they may have become more or less immune to the inland mosquitoes of their own districts. These facts clearly indicate that there is a specific difference in the poison of different kinds of mosquitoes, and Dr. Smith's experiences show that acquired immunity to one mosquito may give little or no relief from another.

There is a popular belief that if a mosquito is allowed to draw his fill of blood, the bite is less painful and becomes less swollen than if she is killed or driven away. This belief is to a large extent true, the probable reason being that when the insect is allowed to finish her meal, the droplet of poisonous saliva injected into the wound is drawn back into the stomach of the mosquito with the blood on which it acts.

Many different remedies have been recommended for mosquito bites. Ammonia, alcohol, glycerine, indigo, iodine, ether, camphor, naphthalene, cresol preparations, a $2\frac{1}{2}\%$ carbolic solution — all these and others have had their adherents amongst entomologists, hunters, travelers and housewives. All of them probably have some alleviating effect, and it is not unlikely that their effects may vary with different species of mosquitoes and perhaps even with individuals. Dr. Howard found that moist soap rubbed on the bites was the most satisfactory remedy in his own personal experience. Ewing found strong alcohol or strong ammonia to be most effective. He observed that if mosquito bites are rubbed the itching is at first increased, but if vigorously practiced all the swelling disappears, and with it the itching, in from $\frac{1}{3}$ to $\frac{1}{2}$ the normal time.

Probably no remedy or disinfectant, no matter how quickly applied after an infected mosquito has been sucking blood, would be effective in preventing infection with malaria, yellow fever or dengue. *Filaria* and *Dermatobia* infections, however, could probably be prevented in this manner, since it takes an appreciable time for the larvæ to enter the skin in the vicinity of the wound.

Control and Extermination

The control of mosquitoes may be undertaken in the following ways, in reverse order of permanent usefulness: (1) personal protection by the use of repellents on or near the person, or of protective clothing; (2) the elimination and exclusion of mosquitoes from dwellings or their diversion from houses by domestic animals; (3) the local destruction of larvæ by the use of temporary "larvicides"; (4) the prevention of breeding by obliterating breeding places or making them uninhabitable.

Personal Protection. — This method of dealing with mosquitoes has no permanent value whatever, and does nothing to lessen the number of mosquitoes, but it is indispensable to the hunter or visitor in mosquito-infested places. Concerning the use of protective clothing, little need be said; the value of gloves, veils, high boots, leggings, etc., is obvious.

The use of "mosquito dope," or ointments repellent to mosquitoes, on the exposed skin is a popular but usually disappointing safeguard against attacks by these insects. The number of popular repellents for mosquitoes is as great, if not greater, than the number of popular applications for the bites. Nearly all of these are unquestionably effective while they last, but they all have the disadvantage of losing their power by evaporation in a short time, and therefore have to be renewed at frequent intervals. Spirits of camphor, oil of pennyroyal, oil of peppermint, lemon juice, vinegar, anise oil and oil of citronella are all effective protectors while they last. Oil of citronella has been most widely used in America. This mixed with an equal amount by weight of spirits of camphor and half as much oil of cedar is a mixture recommended by Dr. Howard, and one which I have used with good results. A few drops of this mixture poured on a bath towel at the head of a bed, and a little rubbed on the face and hands if the mosquitoes are very persistent, was found by Dr. Howard to last long enough through the night to be effective against all mosquitoes except the yellow fever species, *Aëdes ægypti*, which begins its attacks at daybreak.

Elimination and Exclusion from Buildings. — The second means of controlling mosquitoes, by eliminating and excluding them from dwellings, is of more permanent value than the first, and should never be omitted while the process of mosquito extermination is under way. Hospitable housewives who offer in their homes to anopheles such attractive luxuries as cobwebs, dust, and dark damp corners should be brought to regard the presence of gorged sluggish anopheles in much the same light as cultured people now regard bedbugs and lice. They should be destroyed or at least put to all possible discomfort by cleaning and whitewashing.

One of the best methods of ridding houses of mosquitoes after they are once in is fumigation, and this is also an indispensable method of destroying hibernating mosquitoes in cellars, attics, barns, etc. The substance used for fumigation must depend on the kind of place to be fumigated, and on the conditions under which it is done. The most thorough and certain method of fumigation, when the place to be fumigated can be vacated, is by the generation of hydrocyanic acid gas. A less dangerous and equally effective method, but one which is injurious to metals and house furnishings is by the use of fumes of burning sulphur. These methods of fumigation are described in Chapter XXIII, pp. 456–460.

Fumigants which are not dangerous to human beings can be used effectively against mosquitoes since these insects do not require such penetrating fumes as are necessary to destroy hiding parasites, as bedbugs and lice. Pyrethrum or Persian insect powder, manufactured out of the dried flower heads of certain species of chrysanthemums, is an effective fumigant of this type; it can either be dusted into corners, blown into the air of a room, or burned. Powdered jimson weed, *Datura* *stramonium*, is recommended by Dr. Smith, eight ounces, mixed with one-third its weight of niter or saltpeter to make it burn more readily, being burned per 1000 cubic feet. " Mimm's Culicide " is a volatile liquid made of carbolic acid crystals and gum camphor in equal parts by weight, which is effective against mosquitoes, four ounces being volatilized by heating for every 1000 cubic feet of space. A fumigant which has come into great favor in the last few years is cresyl; 75 grains to 35 cubic feet is sufficient to kill all mosquitoes, and in this dilution it is not injurious to man or other higher animals. It is not injurious to metals or to household goods. Various proprietary compounds such as " Flit " and " Fly-tox " sprayed in the corners of a room with a spray-gun are very useful.

In camps which are not mosquito proof, the only effective means of obtaining comfort is by the use of smudges as described for blackflies (p. 526).

Protection of houses against mosquitoes is almost a necessity in many places. To a certain extent the construction of a house affects the number of mosquitoes attracted to it. Light, airy rooms with white walls are much less infested with mosquitoes than are dark, damp houses. Ross says that houses decorated with curtains, pictures, stuffed chairs and similar " barbarous " furnishings are entirely inappropriate for the tropics, and he deplores especially the use of curtains since they " check the breeze which is so cooling to the inmates and so unpleasant for mosquitoes."

The careful screening of houses or rooms is highly valuable, especially in places where mosquito-borne diseases are prevalent. Mosquito net or screen should never be less than 18 meshes to the inch. Cloth net is more effective than coarse wire, since mosquitoes cannot as readily force their way through, but even when stretched tightly it excludes the breeze in hot weather. The use of tight canopies over beds is extensively practiced in some countries, and these are very commendable when kept in good repair and if the discomfort resulting from exclusion of a breeze can be tolerated. The American system of tightly screening doors and windows with wire screen is infinitely superior to the use of bednets in unscreened houses as practiced in India and many other tropical countries. Fairly good protection can often be obtained by keeping a fan going immediately over a bed. Most firms dealing in camp outfits place on the market light folding frames covered with mosquito netting for use when resting or sleeping out of doors in mosquito-infested places.

Usually a few mosquitoes find their way into screened rooms in spite of the screens, through unnoticed crevices, opening of doors and the like. These can usually be discovered and destroyed with a fly spanker, or, what is just as effective in case spotting the walls with blood is to be avoided, by holding a cup of kerosene directly under them. The mosquitoes are stunned by the vapor and fall into the cup in a few seconds. Mosquito traps have been found useful in some places, these contrivances consisting merely of a box, dark colored inside, placed where it will readily be found by mosquitoes and utilized as a hiding place. The box is arranged so that the insects do not readily find their way out and so that it can be fumigated easily.

As already pointed out, cattle kept in or near houses may serve as a protection of the inmates from certain anopheles, and the existence of dark, damp cattle sheds between a house and a breeding place may afford almost perfect protection against certain kinds of malaria mosquitoes, but is of no use for species which do not prefer animals to man. In a similar way a chicken house may serve to divert *Culex quinquefasciatus.*

Larvicides. — Far more effective and satisfactory in every way as a method of coping with mosquitoes is their actual extermination, not necessarily in a whole continent or a whole country, but in local places. Only comparatively recently has the local extermination or even reduction of mosquitoes ceased to be looked upon as too vast an operation to be undertaken. Because ponds or marshes were known to exist, perhaps miles away, the value of destruction of such breeding places as rain barrels, tin cans full of water, cesspools, ditches and troughs was looked upon as a mere drop in the bucket. Knowing as we do now that in most cases every annoying mosquito which attacks us was born and bred within a few hundred yards of where we meet her, the local extermination of mosquitoes has taken on a very different aspect. It is difficult for the uninitiated to realize that the mosquitoes which make life miserable for him did not travel from distant marshes and ponds but were often bred in his own backyard or in his own living room.

Wonderful results have been obtained by the destruction of larvæ in their breeding places. Several methods for accomplishing this have been developed, the most important ones being the use of oil films, the use of substances which poison the water, and the dusting of Paris green on the surface of water, the latter being useful only for anopheles larvæ, which are surface feeders.

Oil films on water destroy mosquito larvæ by plugging up the openings of the breathing apparatus, and thus suffocating them. Surface tension prevents water from entering the spiracles, but droplets of oil act differently and readily enter, plugging up the main tracheal tubes.

For small bodies of water which cannot easily be drained or stocked with larva-eating fish, the oil film method is a valuable one. Except for wind-swept bodies of water ordinary kerosene or petroleum is satisfactory, but the film is so thin and light that it is easily blown aside leaving uncovered expanses of water, and it evaporates quickly. Thick heavy grades of oil do not spread on water, especially if obstructed by water weeds. Waste oil drained from automobile crank cases is usually deficient in spreading power, but this can be rectified by adding kerosene. Howard, Dyar and Knab recommend a grade known as " light fuel oil " for ordinary use. About an ounce of petroleum to 15 square feet of water gives satisfactory results and produces a film which lasts for 10 days, but some heavier mixtures, if they spread, are advantageous in lasting longer. Various methods of application are used. For small pools, barrels for fire protection, etc., it can be poured on; in larger ponds it is better sprayed or spread by means of petroleum-soaked mops. Small streams can be supplied with a continuous film by the use of oil-soaked waste cloth so placed that the slow-flowing water will take a film from it, by means of drip barrels placed over the stream, by means of weighted conical containers in the water from which the oil can escape slowly, or by sacks of oil-soaked sawdust anchored under the water. When the oil is exhausted the sacks can be dried and used over again. A series of vertically-placed planks in a slow-flowing stream facilitates the maintenance of a continuous oil film.

In the tropics the use of petroleum has often been found impracticable on account of the rapid evaporation, continued heavy rains, and the interference made by the luxuriant and rapid growth of water plants and algæ and the formation of an interfering scum from a combination of the oil and dead algæ. For this reason substances which are actively poisonous to the larvæ and which form an emulsion in the water are used instead. An almost ideal larvicide of this type is now made at Ancon, C. Z., in enormous quantities. It is made of crude carbolic acid, powdered resin and caustic soda, heated together to make a black liquid resin soap which readily forms a milky emulsion with water. It destroys anopheles larvæ in 16 minutes in an emulsion of one part in 5000. It also kills larvæ in mud, and destroys grass, algæ and water weeds in which larvæ ordinarily hide. Recently cresol has been advocated as a larvicide, dilutions as low as one part per million being said to be fatal in a short time.

Creolin is also highly recommended as being more effective and cheaper than oiling under tropical conditions; it is said to kill larvæ in dilutions up to 1:20,000. Many other poisons have been tried, such as copper sulphate, mercuric bichloride, etc., but these are not as useful as the oils and emulsions. In Texas a substance known as niter cake, a manufacturing waste product containing sulphuric acid, has been found very useful in wooden fire barrels and some other types of containers. Roubaud found powdered paraform sprinkled on water to be specifically effective against mosquito larvæ. In the Orient the powdered roots of various species of *Derris* have been found to have a poisonous effect both on insects and fish, and similar effects of powdered *Chara* of various species on mosquito larvæ have been recorded by some observers but not confirmed by others. There is a difference of opinion as to whether water in which *Chara* grows is injurious to mosquito larvæ. Matheson and Hinman (1929) got evidence that a vigorous growth of *Chara* is not only injurious to larvæ but prevents eggs from being deposited, but as soon as any decay sets in the inhibiting effect is lost. They correlate the effect of *Chara* with a high oxygen content of the water. Recently Matheson has observed that borax in a concentration of 1.5 to 4 grams per liter kills mosquito larvæ, and he thinks this has excellent possibilities for destruction of mosquitoes in cisterns, barrels, etc., of water not to be used for drinking.

In recent years the dusting of water with Paris green has come into extensive use. The Paris green is diluted by mixing with some inert dust such as road dust, coir dust, hydrated lime, sawdust, etc., in various proportions from 1:1 to 1:100 according to the locality and method of distribution. The grains of Paris green float on the surface of the water, eventually sinking after a number of hours. Meanwhile, however, they are devoured by the surface-feeding anopheles larvæ, and the latter die. The amount of Paris green required varies with the amount of vegetation or other obstruction; in open waters 1 lb. per 20 acres is effective, giving an average of 10 granules per square inch, but where the surface is more or less obstructed by vegetation as much as 1 lb. per acre may be required. The dust can be satisfactorily spread by hand-throwing only in small bodies of water. Where breeding occurs mainly around the vegetation covered margins of reservoirs or streams, dusting by means of a bellows or sprayer is satisfactory. For large marshy or swampy areas, tidal pools, or other extensive breeding places dusting from aeroplanes has been found very convenient and highly effective. An aeroplane flying at right angles to the wind can distribute the dust effectively over strips several hundred yards in width, depending on the flying height and the amount of wind, which should not be over about 4 miles an hour. The effectiveness of the treatment is tested by placing pans containing anopheles larvæ in scattered typical locations. The dust successfully filters through water vegetation and even trees, though of course larger quantities are then required. The effects are much superior to oil in that no injury is done to any inhabitants of the water except anopheles larvæ, — other water insects, fish, plant life, etc. appear uninjured in contrast to the obnoxious appearance of oiled waters. Rice fields in which the rice is still young can be treated very effectively with Paris green, which does not injure the young plants. However, few other mosquito larvæ are killed, and pupæ are uninjured, and within a few hours after treatment breeding can begin again, thus necessitating more frequent treatments. Griffitts has recently reported some success in destruction of salt marsh mosquitoes by mixing Paris green with wet sand and distributing it by aeroplane, thus carrying it to the bottom where the *Aëdes* feed upon it.

Prevention of Breeding, and Natural Enemies. — The most valuable method of reducing mosquitoes, where practicable, is to obliterate breeding places or to make them uninhabitable for the larvæ. The first step in reducing mosquitoes is to see that there are no flower-vases or other water receptacles serving as aquaria for the larvæ, that there are no water-filled tin cans in the garbage heap or that the roof or street gutters do not hold standing water. Any rain barrels, cisterns, cesspools or small reservoirs which cannot be disposed of can be made harmless by screening.

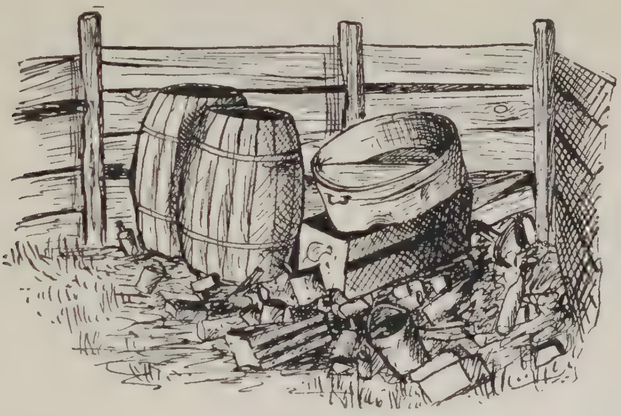


FIG. 293. One of the first places to clean up in a mosquito campaign. A favorite breeding place for such annoying or dangerous species as the yellow fever mosquito, *Aëdes ægypti*, the house mosquitoes, *Culex pipiens* and *C. quinquefasciatus*, *Anopheles quadrimaculatus*, and others.

For prevention of breeding of anopheles drainage measures are often necessary. Not only must small pools of standing water be eliminated but the drains themselves must be made unsuitable for anopheles breeding. In some cases other methods of control, such as filling in of depressions, stocking of ponds with fish, or protection of swamps by means of levees, dikes or tide gates are more practical. Drainage ditches, with narrow bottoms, the sides of which are kept clean and straight, preferably by cement or board walls, are the best means of draining borrow pits, swampy depressions in streams, or outcrops of seepage water. The latter are the most difficult and often have to be drained by ditches which more or less follow the contours, ultimately connecting with main ditches leading away. Lined ditches cost more to build but are more permanent, more easily kept clean, and cheaper in the long run. Subsoil drainage by means of tile or pipe is often necessary; in the Malayan hills Watson got wonderful results by thus draining ravines where *A. maculatus* breeds, and excellent results have been obtained from this method in Panama also. Where water is held at the surface by an impervious stratum overlying a pervious one vertical drainage may be successful, by drilling holes through which the water can flow down to the deeper pervious strata. Salt marshes may be drained by appropriately placed drains, averaging 200 to 300 ft. to the acre, as successfully done by Headlee in New Jersey, with filling in of parts which cannot be so drained; the falling of the tide carries the water out of the ditches. When the tide is insufficient to do this, engineering projects of diking, with tide gates, must be resorted to; the tide gates are to let out water from streams or ditches and after high tides, and also to allow water to enter at intervals in order to prevent excessive shrinking of the marsh land, which sometimes necessitates expensive pumping operations.

The natural enemies of mosquito larvæ can often be exploited successfully for destroying them. Dr. Smith found that one of the most potent factors in the reduction of mosquitoes in the great tidal salt marshes of the New Jersey coast were the various species of killifish, Cyprinodontidæ. These fish abound wherever the marshes are constantly flooded and push into places where there is barely enough water to cover them, and are so active in destroying mosquito larvæ that the latter can exist only in high-lying or shut-in portions of the marsh over which the tide only occasionally sweeps and to which the "killies" do not penetrate. Knowing the value of killifish as destroyers of larvæ, the problem of preventing the marshes from producing countless mosquitoes resolves itself into so draining that the water on it either will be drawn off at every low tide or will be constantly stocked with fish. A number of workers have recently remarked on the folly of oiling pools which could be stocked with fish, since the oil kills the natural enemies of the larvæ and is not permanent. Instead it is urged that fish be propagated in such pools. The water weeds, however, should be removed and overhanging plants cut back so that the fish can operate freely in their pursuit of larvæ. The larvæ have remarkable protective instincts and escape the fish by hiding in or over vegetation or other objects in the water if they are available. Swamps converted into pools in their deepest parts can often be controlled by fish. Fish have been successfully used even in open cisterns and exposed wells. Many progressive towns have hatcheries from which mosquito-destroying fish can be obtained.

The viviparous *Gambusia affinis*, widely distributed in southeastern United States, is one of the most valuable species on account of its hardiness and ability to live in both fresh and brackish water, but many other species serve equally well in localities where they thrive. Farther north the barred killifish, *Fundulus heteroclitus*, of brackish water, and *H. diaphanus* of fresh water are valuable species. An especially useful fish in the tropics is one known as "millions," *Girardinus pœciloides*, which has been extensively introduced into many parts of the tropics from its home in the West Indies; it thrives nearly everywhere if not destroyed by larger fish. In northern Italy a cyprinid fish of the genus *Leuciscus* has been found very valuable. Many other small insectivorous fish are also useful, including gold fish, and the young of many larger fish, collectively known as "minnows," nearly always keep waters in which they are abundant free of mosquito larvæ if their operations are not interfered with by dense vegetation.

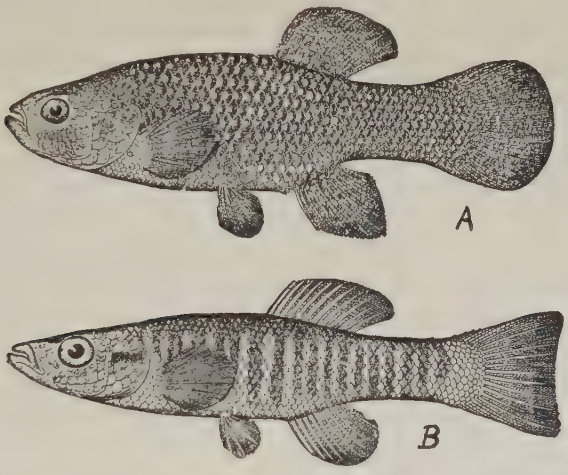


FIG. 294. Some good natural enemies of mosquitoes; *A*, common killifish, *Fundulus heteroclitus*, of great value in brackish marshes; *B*, fresh-water killifish, *Fundulus diaphanus*, valuable in fresh-water streams and ponds. ¾ nat. size. (After Jordan and Evermann.)

Other natural enemies of the larvæ besides fish might well be encouraged in ponds or reservoirs. The western newt or water-dog, *Notophthalmus* (or *Diemyctylus*) *torosus*, which is abundant all along the Pacific Coast of the United States, has been observed to feed very largely on larvæ. In Oregon I have observed grassy pools, which were otherwise ideal breeding places for mosquitoes but which contained numerous water-dogs, absolutely free of larvæ, whereas other pools not a quarter of a mile distant in which no newts were found were swarming with larvæ and pupæ. Experiments by the author have demonstrated conclusively that this salamander can be utilized successfully to keep mosquito larvæ out of such receptacles as rain barrels, troughs, etc. Recently Matheson has made similar observations on the eastern newt.

There are many other water inhabitants which attack mosquito larvæ, such as predaceous beetles and bugs; the large Belostomid water-bugs are commonly sold in Chinese shops in Malaya. Some birds, especially ducks, may also help in keeping larvæ out of ponds.

Many birds feed actively on adult mosquitoes, especially night hawks, swifts and swallows. Bats have been exploited as mosquito destroyers, and the erection of a municipal bat roost has actually been done in San Antonio, and recommended for other places, but scientific investigation has not substantiated the extravagant claims made for the efficiency of bats as mosquito destroyers, and there is no basis for believing that bats can be relied upon for this purpose, except possibly under exceptional conditions.

It is probable that in the tropics wall lizards or geckos and jumping spiders destroy a sufficient number of mosquitoes in dwellings to be of real benefit.

CHAPTER XXVIII

FLY MAGGOTS AND MYIASIS

General Account. — Disgusting as it may seem, the human body is attacked not only by the numerous adult flies discussed in the last chapter, but is subject to attacks or invasion by the maggots or larval stages of some species of flies. Such an infestation by fly maggots is commonly known as myiasis, intestinal myiasis being the presence of fly larvæ in the intestine, cutaneous myiasis in the skin, etc. Although the larvæ of Diptera are nearly always the cause of such infestations, they do not have an absolute monopoly. Casazza (1928) has observed, in Italy, two cases of human infestation with a species of Coccidæ or scale-insects, which he called *Dermolecanium migrans.* One case resembled scabies, while the other resembled cutaneous myiasis. Iyengar (1928) has called attention to frequent infestations with small adult dung beetles (Scarabæidæ) in children in Bengal, the beetles probably entering through the anus.

All of the maggots which habitually or occasionally parasitize man belong to the order Diptera, and to the suborder Cyclorrhapha, in which the larvæ have very small and indistinct heads, and the pupæ are inactive oval bodies from which the adults emerge by pushing off one end, like a cap (see p. 504 and Fig. 236).

Most cases of myiasis are caused by flies quite closely allied to houseflies, and this famous transporter of germs and filth is itself occasionally guilty. The identification of maggots is often a difficult matter and is sometimes impossible without rearing the adult insect. Larvæ of the botfly family, Œstridæ, are of various shapes, but seldom taper evenly from the posterior to the anterior end; the body has a leathery covering and is armed with girdles of thornlike spines. Larvæ of the genus *Fannia* (Fig. 307) are flattened, and have very characteristic fleshy processes along their sides. Nearly all other maggots causing myiasis are cylindrical, whitish, footless creatures, tapering from the broad posterior end to the small head, and are difficult to identify. The chief characteristics used for distinguishing them are the number and form of the mouth hooks (see Fig. 305), and the nature of the respiratory openings at the posterior end of the abdomen. These openings consist of two " stigmal plates," hardened, yellowish, eyelike spots, in which are three slits or openings, with sometimes a button-like mark at their base. The relative position of the stigmal plates to each other and to the surface of the larva, and the form of the slits, whether straight, curved or wavy, and whether vertical or oblique, are some of the characters used in distinguishing genera and species of fly maggots. A few typical forms are shown in Fig. 295.

It is more convenient to consider the different types of myiasis according to the way in which the larvæ attack the body or according to parts affected than according to the families and genera to which the flies belong. We may divide the various flies causing myiasis into four groups: (*a*) those in which the larvæ live outside the body and suck blood by puncturing the skin, (*b*) those in which the larvæ burrow into the unbroken skin and develop under it, (*c*) those in which the eggs or young larvæ are deposited in wounds or in natural cavities of the body, such as the nose, ears and vagina; and (*d*) those which live in or pass through the intestine or urinary passages.

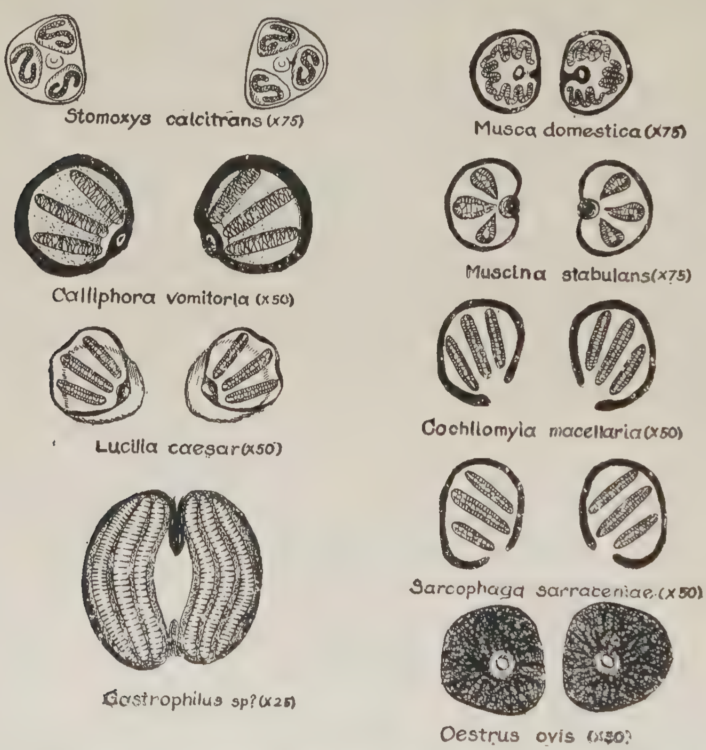

Stomoxys calcitrans (x75)
Musca domestica (x75)
Calliphora vomitoria (x50)
Muscina stabulans (x75)
Lucilia caesar (x50)
Cochliomyia macellaria (x50)
Sarcophaga sarraceniae (x50)
Gastrophilus sp? (x25)
Oestrus ovis (x50)

Fig. 295. Posterior stigmata and breathing pores of various maggots. Note distance apart of opposite stigmal plates, form and position of spiracles, presence or absence of button, etc.

Blood-Sucking Maggots

A number of species of flies allied to the blowflies are known to deposit their offspring in the nests of birds, where the maggots attach themselves to the nestlings and suck blood. The only species of fly in which the larva sucks blood by puncturing the skin of man, however, is the Congo floor maggot, *Aucheromyia luteola* (Fig. 296), found throughout tropical Africa south of the Sahara Desert. Its range closely coincides with that of the Negro and Bantu races of men; it does not occur in countries inhabited by Arabs and Berbers.

The adult fly (Fig. 296*A*) resembles the blowfly, to which it is nearly related. The color, however, is different, being a dirty yellowish brown with the tip of the abdomen rusty black. This fly can usually be observed in shady places about human habitations, preferring the vicinity of latrines; it feeds principally on rotting fruits and on excrement. The female lays her eggs during the daytime in dust or débris in shady places, especially on the floors of native huts. The fly is said by Roubaud to make a furrow in the dust with her abdomen while running on the ground, feeling for breaks or cracks in which to deposit her eggs. Having found such a spot she forces her abdomen into it and deposits usually a single egg, then seeks a new crack, deposits another egg, etc., until the whole number of from 30 to 80 eggs has been disposed of. The eggs, the development of which is favored by dry surroundings, hatch in a few days. Within four or five hours after emergence the larvæ are ready to suck blood if opportunity presents itself, but they are able to live nearly a month without food, remaining buried an inch or so in the dust of floors. They can always be collected by digging with the point of a

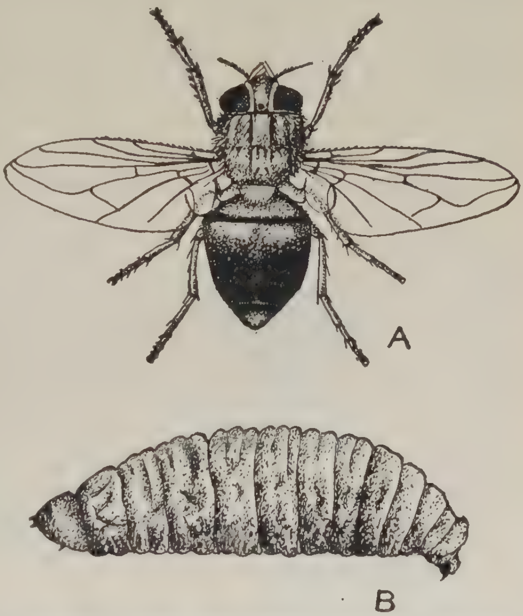


FIG. 296. Congo floor maggot and adult female fly, *Aucheromyia luteola*. *A*, × 3; *B*, × 4. (After Manson.)

knife in cracks in the earth under sleeping mats. Roubaud collected 100 larvæ in half an hour, many of them filled with blood, in a hut where a dozen children slept.

The maggots (Fig. 296*B*) are dirty-white creatures, much wrinkled in appearance, but otherwise quite like the larvæ of houseflies. The tapering anterior end of the body is provided with a pair of black hooks to aid in piercing the skin of the host, and has retractile sucking mouthparts. The thick leathery skin and the position in a crack in the ground protects the larva from injury when stepped on by the bare feet of the natives. The body is beset with rings of spines which aid in the wriggling method of locomotion. The maggots are inactive in the daytime, but come forth at night to suck the blood of sleepers, biting them usually on the side of the body next to the ground. The bites are less irritating than those of mosquitoes, and according to Roubaud the bites of 20 larvæ at once produced no inflammation or itching.

Under ideal conditions the larvæ pass through two moults and go into the pupal stage in 15 days, but this may be extended to about two and one-half months under unfavorable conditions, such as low temperature and irregular food supply. The pupal stage lasts about 11 days. The adults do not begin laying eggs until about two weeks after emergence. The whole life cycle, therefore, from egg to egg, is about one and one-half months under favorable conditions.

The Congo floor maggot is not known to attack any animals but man in nature, though a closely allied maggot, *Chœromyia*, lives in the burrows of the wart hog and other hairless mammals. Its bite is more painful to man than is that of the normal human parasite.

The attacks of the floor maggot can very easily be avoided by sleeping on mats or beds raised just a few inches from the ground.

Maggots Under the Skin

There are several species of flies of which the larvæ burrow into the unbroken human skin, and develop under it, as do " warbles " in cattle, but those which habitually parasitize man are found only in Africa and tropical America. Other forms, including the warble flies, which only exceptionally attack man, are found in other countries. The American skin maggot, *Dermatobia hominis*, is a true botfly, closely allied to the warble flies, whereas the African skin maggot, *Cordylobia anthropophaga*, is a Muscid, closely related to the houseflies and stable-flies.

Dermatobia. — This American fly, sometimes called the human botfly, *Dermatobia hominis* (Fig. 297), is found throughout tropical America from Mexico to northern Argentina. Its larvæ develop not only in man but also in many other animals, as cattle, dogs, hogs, goats, turkeys and, rarely, mules, etc. In certain parts of South America the hides of cattle become so riddled with the perforations made by these bots that they are rendered quite worthless. The infestation in man is contracted chiefly in forest regions, and apparently very seldom in houses, a fact which possibly accounts for the greater degree to which dogs are parasitized by it than are cats, and men than women or young children.

The adult fly (Fig. 297) is about the size of a blowfly (14 to 17 mm. in length) with face and legs yellowish, thorax bluish black with a grayish bloom, and the abdomen a beautiful metallic violet blue. The mouthparts are not fitted for piercing flesh, and there is no " stinger " at the posterior end of the body to drill a hole for depositing the eggs. Evidently, therefore, the many accounts which one can find of the fly's biting or stinging at the time the eggs are deposited are faulty.

The manner in which the larvæ gain access to the skin of their hosts is one of the most remarkable and unusual adaptations known in nature. When ready to oviposit, the female fly captures various species of insects, particularly large mosquitoes of the genus *Psorophora*, but occasionally various other Diptera, and, according to Dunn in Panama, possibly ticks, and glues her eggs by means of an adhesive, quick-drying cement to the under side of the abdomen of these insects. The mosquitoes particularly involved, and a brief résumé of the history of the discovery of this remarkable inter-relation of insects is discussed on p. 578.

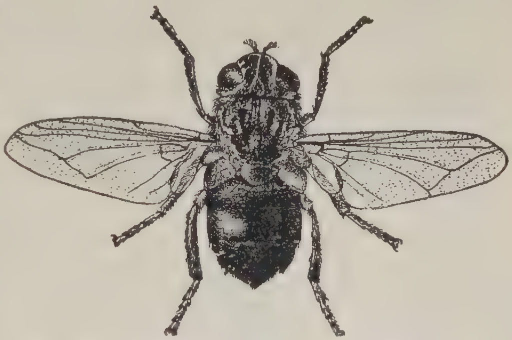


FIG. 297. Adult of South American skin maggot, *Dermatobia hominis.* × 2. (After Castellani and Chalmers.)

When the egg-bearing insects alight upon the skin of warm-blooded animals the maggots emerge, penetrate the skin of the host, several minutes to an hour being required for this process, and begin their development. It is even stated that in case the young larva does not have time to emerge while its mosquito transporter is biting, it withdraws into the egg shell and awaits another opportunity. According to Neiva and Gomes, captive females laid from 16 to 54 eggs on individual flies, and two specimens laid a total of nearly 400 eggs. Eggs frequently found on leaves are probably deposited there by females that have not succeeded in holding flies they have tried to capture, and are compelled to oviposit; such eggs soon die if not kept moist. It has been claimed by da Matta that the flies may sometimes oviposit directly on the skin of the host, but there is no good evidence for this. The eggs require about 5 to 6 days' incubation before the larvæ are ready to emerge.

The time required for the larvæ to reach maturity in the host's skin varies from 5 to 10 weeks. They ultimately reach a length of 12 to 18 mm. (Fig. 298). The anterior end of the larva is broad and is provided with double rows of thorn-shaped spines; the posterior end is constricted, especially in fully-developed larvæ, and does not possess spines. As the larva develops, a sort of boil or cyst forms about it, opening to the surface of the skin by a little pore. This is plugged by the posterior end of the maggot, and used for obtaining air. At intervals these warble-like boils give rise to the most excruciating pain, due, no doubt, to a turning over or moving about of the spiny larva in its close quarters. When mature the larvæ voluntarily leave their host and fall to the ground to pupate. They transform into the adult form in the course of several weeks.

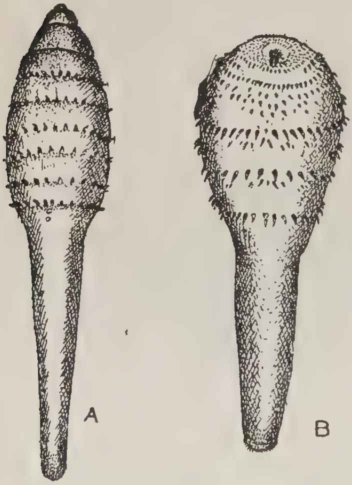


FIG. 298. South American skin maggot, *Dermatobia hominis; A*, dorsal view, extended; *B*, ventral view. × about 3. (After Neiva.)

The swellings under the skin occupied by human botflies, as remarked before, are very painful at intervals, while at other times they are entirely painless. As the larva matures, a puslike material exudes from the open end of the "boil," containing, no doubt, the excretions of the maggot. After the worm has evacuated its cyst or has been removed the wounds sometimes become infected, and may even result in blood poisoning and death. Many calves are killed by secondary infestation by screw-worms.

The method usually employed to remove the maggots is to apply tobacco juice or tobacco ashes to the infested spots, thus killing the worms and making their extraction easy. Another method used by natives in some parts of South America is to tie a piece of fat tightly over the entrance to the boil. The larva, deprived of air, works its way out into the fat, being thus induced to extract itself. A much more satisfactory method of dealing with the worms is to kill them with an injection of weak carbolic acid, mercuric bichloride, or some other poisonous substance, then enlarge the entrance to the cyst with a sharp clean knife and remove the body of the worm. A washing of the wound with a weak carbolic or lysol solution, followed by an antiseptic dressing, obviates any danger of subsequent infection. The wound heals quickly but leaves a scar.

Other Bots. — Other botflies occasionally infest man and cause cutaneous myiasis. The common warble-flies of cattle, *Hypoderma lineata* and *H. bovis* (Fig. 299), have been recorded as occurring in the skin or flesh of human beings and there is one fatal case on record where an ox warble caused an ulceration in the back part of the lower jaw of a boy six years old. In Europe the deer bot, *H. diana*, seems to parasitize man more frequently than the cattle species. Ox warbles gain access to the tissue under the skin of cattle in an indirect way, the hairy bee-like flies depositing their eggs on hairs of cattle, particularly on the legs or flanks. In all, about 800 eggs may be laid by a single female. The odd life cycle, as described by Warburton, is in brief as follows: *H. bovis* deposits its eggs singly at the base of the hairs, *H. lineata*, which is the common form in warmer parts of America, in rows of from 1 to 14. The eggs of *H. bovis* hatch in about 3 to 4 days, those of *H. lineata* somewhat later. The young larvæ, less than 1 mm. in length, are armed with spines on every segment and have a piercing hook flanked by a pair of mouth hooks. They creep down the hair to the skin, penetrate a hair follicle, and disappear under the skin. What happens to them next is unknown, but they evidently wander extensively in the flesh. Several months later they may appear on the esophageal wall, and are now 6 to 14 mm. long, and with the greater part of the body of glassy smoothness. They remain on the move, migrating gradually toward the stomach, and then, usually in the following winter, embark on their last voyage, through the connective tissues, to the subcutaneous tissues of the back of the animal, often pausing on their way in the spinal canal. Many individuals probably pass through the abdominal or thoracic cavities without appearing in the gullet. Entering the hide from beneath, the larva moults and becomes opaque and ventrally spiny, and soon becomes encysted in a "warble," subsisting

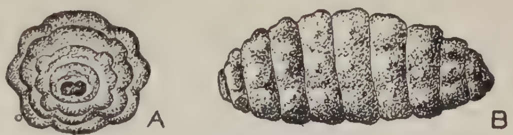


FIG. 299. Larva of *Hypoderma bovis*; *A*, posterior view; *B*, lateral view. × 2.

on the products resulting from inflammation of the walls of the cyst caused by its movements. It next pierces a hole in the skin to admit air, and advances towards it tail first, and then grows rapidly. After another moult the full grown larva, in the following spring, squeezes out through the skin opening, falls to the ground, pupates usually in a hole or crevice, and after several weeks more emerges as an adult fly. Human infestations are comparatively rare, and occur principally on cattle tenders, who probably attract the flies by an odor of cattle.

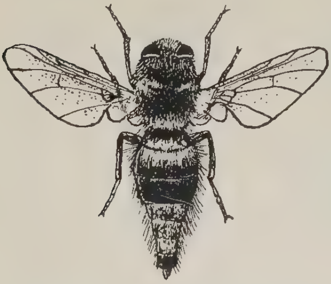


Fig. 300. *Gastrophilus hæmorrhoidalis*, adult female.

In human beings the larvæ, when they reach the subcutaneous tissues, after their travels through the body, sometimes do not immediately settle down and form a " warble " as they do in cattle, but continue their movements just under the skin, producing one form of "creeping eruption." Their travels are then marked by painful red lines which, as they are extended a few centimeters a day, fade out behind in the course of several days. In other instances they form a series of subcutaneous tumors over a period of a number of weeks, between times disappearing in the deeper tissues. In the final tumor a hole is pierced in the skin through which the larva respires as in cattle warbles, until ready to leave the host.

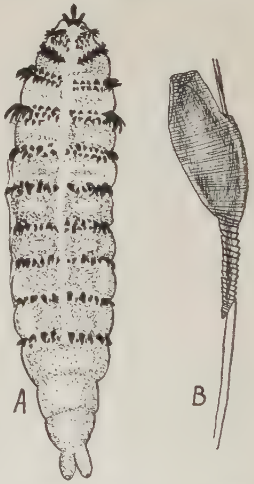


Fig. 301. *A*, newly emerged larva of *Gastrophilus intestinalis*, × 75; *B*, egg of *G. hæmorrhoidalis* attached to hair. After Hadwen (*B* modified).

In Russia a number of instances of " creeping eruption " have been described as the result of infection with horse bots of the genus *Gastrophilus*, which in the normal hosts develop in the digestive tract. It is significant that these cases were due to the species *G. nasalis* and *G. hæmorrhoidalis*, concerning which there is some evidence that the eggs, attached to hairs on the host, hatch spontaneously and burrow into the adjacent skin. *G. nasalis* usually lays its eggs under the chin of horses, whereas *G. hæmorrhoidalis* (Fig. 300) lays them on the lips or occasionally in the nostrils (Fig. 301*B*). The peculiar stalked eggs of the latter species have at times been found attached to human eye lashes or body hairs. *G. intestinalis*, on the other hand, lays eggs which rarely hatch spontaneously, but have to be licked, and the larvæ (Fig. 301*A*) apparently do not penetrate the external skin (see p. 607). This species, therefore, would not be expected as a cutaneous parasite in man.

The tendency to wandering under the skin of abnormal hosts, even by parasites which are not normally subcutaneous parasites at all, is a phenomenon which occurs not only among fly larvæ but also among nematodes, as, for example, *Gnathostoma.* It can probably be interpreted as an effort on the part of the parasites to find situations which are more perfectly adapted to their requirements. When a cattle bot finds its way to subcutaneous human tissue it becomes apparent to it that conditions are not exactly such as its instinct leads it to expect, and it futilely endeavors to correct an error which its parent made when she deposited her eggs.

African Skin Maggots. — The commonest species of maggot which develops in the human skin in Africa is the "ver du Cayor," the larva of the tumbu fly, *Cordylobia anthropophaga.* This fly belongs to the same family as blowflies and screw-worms. It is widespread throughout Africa, from Senegal and Khartoum to the Transvaal. To quote from Fuller, "There is no ill the flesh is heir to among the vicissitudes of life in South Africa, which is more offensive than parasitism by (this insect)." Man is not the main host of the larvæ of this fly, but he suffers in common with a large number of wild and domesticated animals, especially domestic dogs.

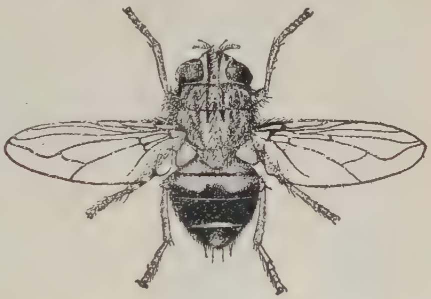


Fig. 302. Adult female of African skin maggot, *Cordylobia anthropophaga.* × 3. (After Castellani and Chalmers.)

The adult fly (Fig. 302) is about the size of a blowfly (7 to 10 mm. long). The head, thorax and legs are straw yellow, the thorax with indistinct dusky stripes, the abdomen with black markings as shown in Fig. 302 in the female, somewhat less extensive in the male.

The flies can be seen darting about in the evening or resting on dark surfaces indoors on bright days. The adults feed on fruits and decaying matter. They are quickly killed by exposure to bright sunlight and by a temperature of about 120° F., but show considerable resistance to cold.

Blacklock and Thompson have investigated the bionomics of this fly. They observed that, contrary to earlier views, the eggs are laid by preference in dry sand previously contaminated with the excreta of animals, though they will sometimes oviposit on cloth, so that clothing left exposed to the flies may be dangerous. When ovipositing in sand the female digs a shallow hole and after laying an egg covers it over with a few sand grains, after which she moves ahead a short distance, plants another egg, etc., at the rate of about 8 eggs per minute. In this way a small area may be thickly sown with eggs. After incubating for 4 days or less the eggs hatch into larvæ (Fig. 303*A*) which are from 0.75 to 1 mm. in length. The more anterior segments are provided with backward-projecting and the posterior ones with forward-projecting spines. There is a pair of mouth hooks which are remarkable in being directed upward, and at the posterior end are a number of finger-like processes. When undisturbed the larva remains hidden in the sand, but on the slightest stimulation by movement or heat it immediately emerges and, sitting up on its tail, so to speak, waves its head about in search of an object to which it can seize. Such larvæ will live for from 9 to 15 days. If successful in attaching itself to a host, it crawls to the nearest wrinkle or crevice, puts down its head, and, using its mouth hooks somewhat like a tack lifter, tears a little hole and lifts the thin superficial skin sufficiently so it can bury itself, which it may do in tender skin in as short a time as one-half to one or two minutes. Once safely covered by the thin layer of epidermis so it cannot be brushed off, it later burrows deeper at leisure. The penetration is painless the first time, but both men and animals who have been attacked before often develop marked skin reactions on subsequent invasions. As in the case of *Dermatobia* an opening is left to the surface of the skin from which the larva obtains air through the spiracles at the posterior end of the body. The imbedded larva moults after about 3 days, and then has a quite different shape and distribution of spines. The second moult occurs on the 5th or 6th day, the larva again having a different appearance, this time being a fat, creamy-white maggot, roughly cylindrical, with numerous small spines, especially on the anterior segments, and with irregular

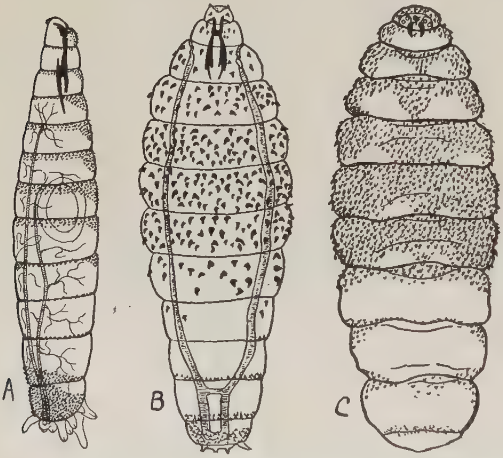


FIG. 303. First (*A*), second (*B*) and third (*C*) stage larvæ of *Cordylobia anthropophaga; A*, × 60; *B*, × 15; *C*, × 4. (After Blacklock and Thompson.)

ventral wrinkles (Fig. 303*B*). It reaches maturity, with a length of from 13 to 15 mm. (Fig. 303*C*), about the 8th day or later, and then leaves the tumor it has occupied in the skin and falls to the ground to pupate, burying itself to some depth. The pupæ, 8 to 10 mm. long, are squarely cut off behind, and have parallel sides; they are at first a light rust color, later turning dark purplish brown. They are resistant to cold and wet but not to high temperatures. The adult emerges in 8 to 10 days.

Roubaud believed that dogs were the natural host of the fly, but Blacklock and Thompson have shown that rats probably serve in this capacity, dogs being very frequently attacked in the wet season, and human beings somewhat less often. The seasonal incidence seems to be due to the flies seeking dry places for oviposition indoors instead of outdoors, and to the tendency for rats to congregate in and around the houses when their burrows are flooded. Young animals or small children are much more liable to infestation than are older individuals, not because of failure of the larvæ to invade the skin, but apparently because of the development of some form of immunity as a result of earlier infections which prevents the larva from successfully continuing with its development. Later experiments by Blacklock and Gordon showed that the immunity is local in nature, at first confined to the skin areas which were previously infected, and gradually spreading to larger skin areas. Larvæ which burrow into immune skin quickly die, yet contact with excised immune skin is apparently not injurious. The immunity seems to disappear, in some cases at least, in the course of a year (see p. 22).

In first infections the larvæ cause no reaction while entering the skin. Subsequently a papule appears which grows in size, reddens, and is slightly irritating. The irritation disappears and later reappears with more severity, enough to cause sharp pain at intervals and to interfere with sleep. The final tumor resembles an ordinary boil, and in severe cases may be accompanied by enlargement of neighboring lymph glands, malaise, and fever. The cavity occupied by the larva is considerably excavated, and there is indication of a dissolving action on the tissues in the vicinity of the head of the larva; often the fluid of the cavity is stained with blood. When heavy infections occur they may even cause death of puppies or rats. As many as 300 maggots have been taken from the skin of a puppy, and even rats sometimes have over 40. In human beings the infestations are seldom so severe, but there are cases of 20 or 30 maggots taken from the scalp of a baby under six months old. Human infection can, of course, result from contact of the skin with infested sand, from clothing on which the eggs have been deposited, especially if they have been allowed to lie on the ground or in the corner of a room, or from sand used in latrines and accidentally spilled on a seat.

Removal of large maggots can usually be accomplished by means of forceps, but smaller ones are best treated by application of liquid paraffin. The larvæ back out into the paraffin searching for air, and by adding more drops of paraffin can usually be induced to emerge far enough so they can readily be removed with forceps or, after lubrication with the oil, by an inward and downward pressure on either side.

A closely allied fly, *C. rodhaini*, sometimes placed in a separate genus *Stasisia*, occurs in the damp equatorial forests of Africa, attacking thin-skinned animals such as antelopes and rodents, and occasionally man, but avoiding thick-skinned animals. Its habits and life cycle appear to be very similar to *C. anthropophaga.*

A few cases of cutaneous myiasis have occurred in North America. Walker has described four cases of the infestation of the otherwise healthy skin of children by *Wohlfartia vigil*, a species belonging to the same family as the flesh flies (Sarcophagidæ). A European species of *Wohlfartia*, *W. magnifica*, attacks wounds and natural cavities of the body, but not the unbroken skin (see p. 605).

Myiasis of Wounds and of Natural Cavities of the Body

A large number of flies, all of them related to the blowflies and houseflies, occasionally deposit their eggs or newly hatched larvæ in neglected wounds or sores when offensive discharges are exuding from them. In like manner they may oviposit in the external ear, nose, eye or other openings, whence the larvæ penetrate to the inner ear, sinuses, or other parts of the body. In severe cases infestations with maggots of these flies may lead to a most horrible and loathsome death.

The flies causing this type of myiasis differ from those previously considered in that they are not always, in fact in most species not normally, parasites. The instinct of the female flies of all the species implicated is to deposit offspring in places from which the odor of meat or of decaying animal matter is emanating, regardless of where the place may be. This instinct is, of course, of the highest value to the species, since the larvæ live upon the substances from which such smells arise. It is an instinct analogous to that which causes a mosquito to lay its eggs in water, or a horsefly to oviposit in objects overhanging water — an unknowing but accurate intuition on the part of the parent to provide for the welfare of its young.

Screw-worm. — One of the most important species in this connection is the American screw-worm fly, *Cochliomyia* (or *Chrysomyia*) *macellaria*, which occurs throughout America from Canada to Patagonia, though abundant only in warm countries.

The adult fly (Fig. 304) is a handsome insect, slightly larger than a housefly, of a metallic blue-green color with three dark stripes on the thorax, and a rather conspicuous reddish coloring of the face.

It belongs to the group of flies which are commonly called blowflies or "blue-bottle" flies, the same family to which the blood-sucking maggots belong. The adults show a marked tendency to congregate about fresh carcasses rather than old ones. They are migratory in their habits, and have been shown to travel at least 15 miles; when seeking a place to deposit eggs they usually travel against the wind, following a scent for considerable distances. Breeding does not begin until warm showery weather comes, and the fly is never abundant in either cold or very dry weather. Few cases of myiasis are caused by it except where the numbers are large, and several generations have already bred out in carcasses. The eggs are laid in batches of from 40 to 250 in the well-known manner of blowflies, fresh batches being deposited at intervals of a few days until over a thousand may have been laid. In warm moist weather the eggs hatch in a few hours, and under the favorable conditions in wounds or sores in a living animal the time is probably as short as three hours. In occasional instances they seem to hatch almost at once.

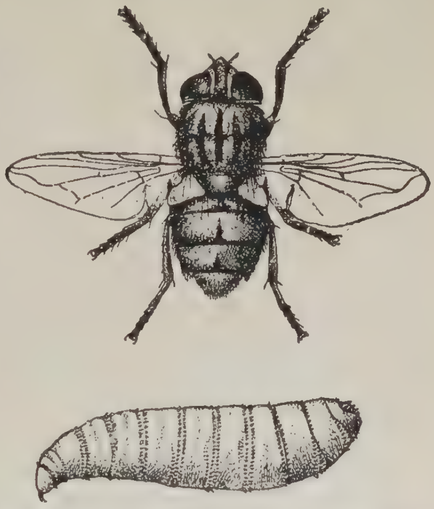


FIG. 304. Screw-worm fly, *Cochliomyia* (or *Chrysomyia*) *macellaria*, adult and maggot. × 3. (Adult after Castellani and Chalmers, larva after Blanchard.)

As soon as the eggs hatch the young maggots, only about a millimeter in length (Fig. 304), begin burrowing into the flesh. They are white, footless creatures, provided with a pair of stout hooks near the mouth, and with bands of minute spines which give them a screwlike appearance, whence they derive their name. Eating away at flesh and even bone, they develop rapidly to a length of 12 to 15 mm., and maturity may be reached in three days, though four or five days is usually required. When fully developed the larva leaves its feeding grounds and buries itself in loose earth nearby, where it pupates in two or three days. The pupæ are brown in color, and shaped somewhat like olives. After four days or more in the pupal case the adult insect emerges, climbs up on nearby herbage and rests in a characteristic position with the head down. The whole life cycle occupies from nine days to two weeks or more.

As remarked before, the female screw-worm fly, about to reproduce, is attracted to any animal smell and frequently finds a suitable place for egg-laying in exposed wounds, or in the nose or ears of people sleeping out doors, especially in case of foul-smelling catarrh. Sometimes the flies select recently vacated *Dermatobia* nests, boils, sores, etc., for the young to develop in. As soon as hatched the maggots begin eating their way into the tissues with which they are in contact, using their strong mandibles as nippers for cutting flesh and even bone. From the ear they may make their way into the inner ear, completely destroying the auditory apparatus. From the nose they penetrate to the pharynx, frontal sinus, the eye-ball, and even the brain, occasionally doing such extensive damage as to cause death. Usually an abundant discharge of pus and scraps of tissue, intense pain, and delirium accompany the infestation.

The injury to the invaded host is not due entirely to the eating away of the tissues, but also to toxic products of secondary bacterial invasion, and possibly of the maggots themselves. Reflex symptoms such as convulsions, visual troubles, loss of speech, fainting, etc. are commonly complained of by the unfortunate victims of the maggots.

The damage done by screw-worms to domestic animals is very great, amounting to millions of dollars in the United States. Wounds made by shears, barbed wire, thorns, ticks, parturition, etc., are commonly invaded, and Stewart has recently called attention to the frequency of myiasis of the cloaca of chickens.

Other Species. — Although the screw-worm is the species most thoroughly addicted to breeding in wounds and natural cavities of the body of man or animals, it is by no means alone in this nefarious habit. The beautifully colored green-bottle fly, *Lucilia cæsar*, and other species of *Lucilia* have this habit, and the common blowflies, *Calliphora vomitoria* and *C. erythrocephala*, are sometimes implicated. These ubiquitous pests are said to have been a great torment to wounded soldiers in the Civil War. A closely related species of screw-worm, *Chrysomyia bezziana*, widely distributed in southern Asia and Africa, is, according to Patton, a very frequent parasite of man and animals in India. From observations on habits and structure, and from experimentation, Patton thinks this species deposits its eggs *only* in living animals. Of the fleshflies, which are related to the Muscidæ, but are placed in a separate family, Sarcophagidæ, many, and possibly all, will at least occasionally breed in wounds or natural cavities of living bodies.

A particularly frequent offender is the black blowfly or wool maggot, *Phormia regina.* This is a large, blackish-blue fly which occurs particularly in cool weather; in southern United States it is abundant both before and after, but not during, the screw-worm season, and does much damage by " blowing " wool, especially in damp weather. It frequently invades the heads of animals when there are wounds around the horns. Human cases seem to be rare but Stewart has described a severe infestation of the scalp, a fly of this species apparently having been attracted by some scalp sores from which foul-smelling pus was being discharged. After a medical application to the scalp the mass of living larvæ behind the ears became so great that they could almost have been spooned out.

A very troublesome species in Europe, especially in Russia, where it is almost as much of a scourge as is the screw-worm in America, is the fleshfly, *Wohlfartia magnifica.* In Russia during hot weather this fly attacks the nose, ears, mouth, sores, wounds of any kind, or even the eyes, of human beings. In one case 70 maggots were extracted from one eye after about this many had already escaped and been thrown away. This fly, unlike most of its allies, is said to attack only living animals. The larvæ are unusually resistant to substances which readily kill other insects; they will survive two hours in 95% alcohol, and 10 minutes in turpentine or pure hydrochloric acid. This species is said to be a great pest in war, where it causes myiasis in the wounds of soldiers. In France it is said to have added much to the sufferings of wounded men.

Other fleshflies occasionally deposit their eggs on living animals or human beings. *Sarcophaga carnaria* is particularly likely to deposit eggs or larvæ in the vagina when it has access to it. As in the case of the flies mentioned above, this species will readily attack the nose or ears, especially if there is a foul-smelling catarrhal discharge flowing from it, and will infest inflamed or diseased eyes, sometimes nesting in large numbers under the eyelids and eating away the cornea.

The fleshflies are mainly gray in color, with longitudinal dark stripes on the thorax and a checkered abdomen which is changeable in varying lights. In summer the smell of decaying flesh will invariably attract them. The checkered abdomen and the broad angle at which the wings are held serve to distinguish them from other gray flies. Their life history is essentially the same as that of the screw-worm fly.

Another fly which must be mentioned in this connection is the sheep head-maggot, *Œstrus ovis*, a species of botfly. It normally lays its eggs in the nostrils of sheep, from which place the maggots burrow into the frontal sinuses. In Algeria it is said to lay its eggs while flying without alighting, upon the eyes, nostrils and lips of shepherds, especially those whose breath smells of fresh sheep or goat cheese. It somewhat resembles a housefly, but is larger and of a warmer brown color. Its mouthparts are deficient to such an extent that the fly is incapable of feeding, its only instincts being those connected with the reproduction of its kind.

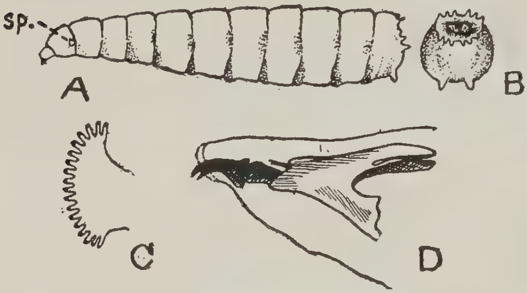


Fig. 305. Larva of fleshfly, *Sarcophaga; A*, side view of larva; *B*, posterior view showing posterior spiracles in depression; *C*, anterior spiracle, marked "sp." in Fig. *A*; *D*, skeleton of pharynx, with mouth hooks. (After Riley and Johannsen.)

Another Œstrid fly which attacks man is *Rhinœstrus purpureus*, so named on account of its purplish hue. It is common in Russia and Siberia, and occurs in various parts of Central Europe. The eggs hatch in the body of the parent, and the tiny maggots are normally deposited, 8 to 40 at a time, in the eyes or perhaps the nose of horses, whence they migrate to various parts of the head or throat of their hosts. Portchinsky states that Siberian peasants are not infrequently attacked by this fly, which rapidly darts toward the eye and deposits its young in that organ. The young maggots cause severe pain so that the eyelids cannot be opened. Unless they are removed they cause ulcerations of the conjunctiva and a purulent exudation. Their removal is effected by dropping cocaine into the eye and then extracting them with pincers or washing. In Norway and Russia cases of myiasis of the eye caused by *Hypoderma* have also been recorded.

Treatment. — The danger arising from attacks of screw-worms and flies of similar habits is that the infestation is often not discovered until too late. Even when one is aware of an attack by the fly, it is not always possible to drive it away soon enough to prevent the eggs or maggots from being deposited. The larvæ should be removed as speedily as possible since they may do a great deal of damage in a very short time. Usually the maggots may be induced to release their hold and to fall out by douching the infested part of the body with a 20% solution of chloroform in sweet milk, or with a carbolic or lysol wash. Even salt water is often effective in removing the maggots and should be used if no better wash is at hand. Maggots in the ear, if outside the ear drum, should be removed by means of water or milk saturated with chloroform or carbon tetrachloride, but if they have already pierced the ear drum, surgery will probably be necessary. Often where infections are two or three days old surgery must be resorted to and the larvæ removed by means of curved forceps. Frequent antiseptic washes prevent the injuries made by the maggots from becoming infected with bacteria.

Control. — One of the most important measures against these wound-infesting flies is the burning of carcasses to prevent breeding, since a single dead cow may breed out a million or more blowflies. Poisoning is also sometimes resorted to, either by poisoning a carcass with arsenic or suspending it over a tub of an arsenical solution from which the flies sip after depositing their eggs. Fly traps are also of value.

Myiasis of the Intestine

There are a number of species of fly maggots which may accidentally be taken into the intestine of man and cause trouble there. To quote from Banks, " When we consider that these dipterous larvæ occur in decaying fruits and vegetables and in fresh and cooked meats; that the blowfly, for example, will deposit on meats in a pantry; that other maggots occur in cheese, oleomargarine, etc., and that pies and puddings in restaurants are accessible and suitable to them, it can readily be seen that a great number of maggots must be swallowed by persons each year, and mostly without any serious consequences." Banks gives the following quotation from Walsh, — " Taking everything into consideration, we doubt whether, out of 10,000 cases where the larvæ of two-winged flies have existed in considerable numbers in the human intestines, more than one single case has been recorded in print by competent entomological authority for the edification of the world."

Botflies. — There are some flies of the botfly family, Œstridæ, which as larvæ habitually parasitize the digestive tracts of horses and related animals, and are especially adapted in habits and structure for such larval life. These stomach bots of horses are sometimes separated from other bots into a family Gastrophilidæ. Bots of this type occasionally but rarely develop in man. The commonest species, *Gastrophilus intestinalis* (or *equi*), as an example, lays its eggs on the hairs of horses where they are likely to be licked off. After an incubation period of ten days or so, when these eggs are licked off, the moisture and rubbing of the horse's tongue cause them to hatch at once, and the young spiny larvæ, adhering to the tongue, make their way to the stomach and intestine where they attach themselves and develop to full-grown spiny larvæ, 15 to 20 mm. in length. In the following spring the larvæ let go their hold, pass out with the feces of their host and pupate in the ground. Obviously it could be only by a series of unusual circumstances that these larvæ could gain access to the human stomach, yet a number of cases have been recorded.

Two other common species of *Gastrophilus* occur in horses, *G. hæmorrhoidalis* and *G. nasalis.* The former species, known as the red-tailed bot, lays its eggs on the hairs of the lips of horses, while *G. nasalis,* the chin fly, lays them on the hairs of the skin under the lower jaw. In both cases the eggs appear to hatch spontaneously, unlike those of *G. intestinalis,* and the young larvæ are now believed to burrow into the adjacent skin. As noted on p. 598, the larvæ of these flies occasionally infest human skin, but seem rarely to reach the digestive tract. In their normal hosts they reach maturity in the stomach, duodenum, or rarely the pharynx.

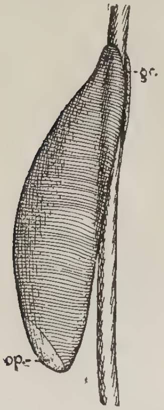


Fig. 306. Egg of horse botfly, *Gastrophilus intestinalis,* attached to hair; *gr.,* groove for cementing to hair; *op.,* operculum. (After Collinge.)

Other Flies Causing Intestinal Myiasis. — A number of different species of flies which normally develop as larvæ in the feces of man or animals may live and grow in the intestine. In most cases such larvæ are not truly parasitic at all, since they merely develop in the contents of the intestine and do not attack the tissues, but they must be regarded as at least potentially dangerous, for they may easily become lodged in positions where they may attack the mucous membranes, and are not then to be trusted to discriminate to the advantage of the host. Even when they do not attack the mucous membranes they may cause much nausea and abdominal discomfort by their movements.

Among the flies which breed in fecal or decaying material, and which frequent houses, and whose larvæ not uncommonly pass through the digestive tract, feeding and growing en route, are some of the species of *Fannia.* *F. canicularis* is often called the "lesser housefly," and is common in houses both in Europe and America; it is frequently seen hovering about chandeliers or hanging near the center of rooms. The peculiar manner of flight, a sudden dart followed by a hovering, is very characteristic and a good means of identification. The eggs are laid in decaying animal or vegetable matter and sometimes in excrement, and may be accidentally ingested with decayed lettuce leaves, bad fruit, etc. It is also possible that the eggs may be laid in or near the anus of people using unsanitary privies, whence the larvæ work their way up into the large intestine. The larvæ (Fig. 307) are very different in appearance from those of houseflies or blowflies, being broad and flattened, about 6 mm. in length when full grown, brown in color, with rows of spiny processes to which adhere particles of dirt and filth. The latrine fly, *F. scalaris*, is very similar to the species described above, but is larger and differs in minor details of form and habits. It prefers excrement, especially human excrement, on which to deposit its eggs, and has gained its common name from its frequent presence about privies and latrines. I have found larvæ of this species very abundant in chicken manure. The adult has the same darting and hovering manner of flight as its close relative, *F. canicularis*. The larvæ (Fig. 307) differ from those of the latter species in the form and arrangement of spines. Several cases are on record in which *Fannia* larvæ were passed in the feces intermittently for a number of years, often accompanied by a chronic disorder of the intestine. It is probable in these cases that repeated reinfections occur.

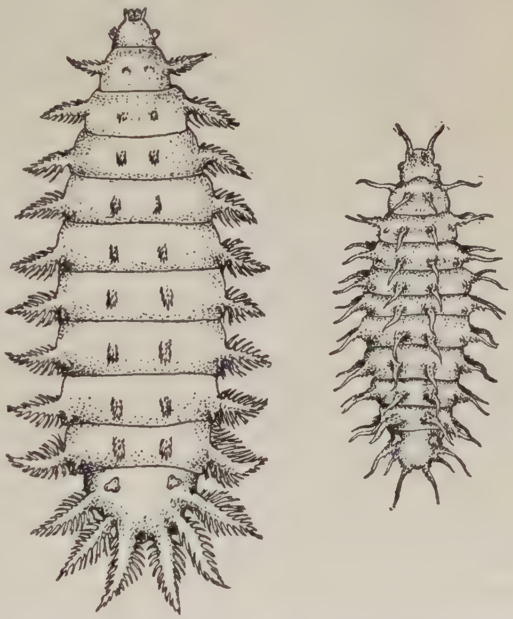


FIG. 307. Larvæ of *Fannia scalaris* (left) and *Fannia canicularis* (right). × 8. (After Hewitt.)

Another common cause of intestinal myiasis is the larvæ of the cheese-fly, *Piophila casei*, popularly called "cheese-skippers" (Fig. 308). These larvæ often occur in abundance in old cheese, and also in ham, bacon and other foods. It is thought by some people that their presence in cheese is an indication of particularly good cheese! These maggots resemble diminutive housefly larvæ, but have two mouth hooks like the blowfly maggots, whereas the housefly larvæ have a single median one. Probably in many cases the cheese-skippers pass through the intestine without doing much damage, but they sometimes attack the mucous membranes, causing bleeding sores which may become infected and ultimately lead to ulceration. Severe pain in the abdomen, headache and vertigo have been known to be caused by these larvæ in the intestine.

The common housefly is also sometimes a cause of intestinal myiasis, especially in young children. In a case which occurred in the Philippines, the walls of the stomach were extensively eaten away by larvæ of this common fly, and 20 or 30 maggots were obtained by means of a stomach pump. A liver abscess which was not due to the usual amebic infection accompanied this case, but whether due directly or indirectly to the myiasis is uncertain. Some of the flesh flies are also sometimes involved. In one recorded instance a Chinaman passed about 50 larvæ of *Sarcophaga fuscicauda* in each stool for eight days.

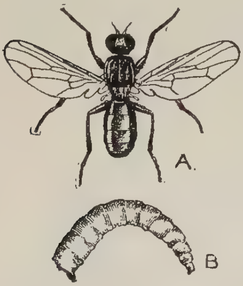


FIG. 308. Cheese-skipper and adult, *Piophila casei.* × 3. (After Graham-Smith from Riley and Johannsen.)

The powerful resistance of fly maggots to substances which would quickly destroy other animals makes it possible for many species to pass through the stomach safely if accidentally swallowed either as eggs or young worms. As said before experiments show that the larvæ of the fleshfly, *Wohlfartia magnifica,* can survive two hours in 95% alcohol, and ten minutes in pure hydrochloric acid or turpentine. It is a little wonder, then, that fly maggots are not destroyed by the 0.2% hydrochloric acid of the stomach or by the other digestive juices.

Effects. — The effects of fly larvæ in the intestine are extremely variable, depending on the heaviness of the infection, the species of flies, and on individual susceptibility. There are many cases where the presence of the larvæ in freshly passed stools is the first indication of their having existed in the intestine, and it is practically certain that the majority of infections are never known or suspected.

On the other hand more or less serious symptoms may be caused by intestinal myiasis. The presence of *Fannia* larvæ or of cheese-skippers in the digestive tract often gives rise to temporary intestinal disturbances, such as loss of appetite, vomiting, general malaise, abdominal pains, diarrhea, constipation and intestinal bleeding. Sometimes headache and vertigo indicate the absorption of toxic substances secreted by the maggots or their entrance to the blood circulation through the wounds. A few cases of death from intestinal myiasis have been recorded, and it is probable that appendicitis may sometimes be caused through injury to the walls of the appendix by fly larvæ which start sores leading to ulceration. Those maggots which pass directly through the digestive tract, feeding only on food substances with which they come in contact en route, do little or no harm to the temporary host. Those larvæ however, which attack the living tissues lining the stomach and intestine are the cause of the symptoms named above.

Fly maggots can usually be expelled readily by means of purges and doses of the drugs which are used for intestinal worms (see p. 212). The chief danger from infection, as in other forms of myiasis, lies in the fact that the presence of the maggots is usually not even suspected until much of their damage has been done. Prevention, of course, consists principally in care as to what is eaten, especially in regard to such foods as raw vegetables and partly decayed fruits.

Myiasis of Urinary Passages. — Myiasis of the urinary passages, both urethra and bladder, is a rare but occasional occurrence. The flies implicated are usually the lesser housefly, *Fannia canicularis*, and the closely allied latrine fly, *F. scalaris*, which have already been described in connection with intestinal myiasis. In most cases infection occurs from eggs laid near the external opening of the urethra, the larvæ working their way up into this tube and even into the bladder; apparently they need very little oxygen. Contamination is favored by sleeping without covers in hot weather, so that flies have free access to the anal and genital region. The larvæ, when escaping, are said to be able to project themselves with a flicking motion to a distance of from 12 to 20 inches.

SOURCES OF INFORMATION

The following list of " sources of information " includes only those periodicals which are at least partly devoted to parasitology and preventive medicine, or which frequently contain important articles on these subjects, and those books which cover the entire subject or parts of it in a comprehensive manner. Books which are out of date and have been superceded by newer ones are not included. Most of the books listed contain more or less extensive bibliographies which should be of great assistance to anyone who desires to pursue any phase of the subject of human parasitology beyond the hallway to which this book may lead him.

PERIODICALS

United States and Canada

American Journal of Hygiene, Baltimore, 1921–
American Journal of Public Health, New York, 1911–
American Journal of Tropical Diseases and Preventive Medicine, New Orleans, 1913–1915. (Merged with New Orleans Medical and Surgical Journal.)
American Journal of Tropical Medicine, Baltimore, 1921–
Index Medicus, Washington, 1879–
International Health Board, Annual Reports and Publications, New York, 1913–
International Health Commission, Rockefeller Foundation, Publications, New York, 1913–1916.
Journal of the American Medical Association, Chicago, 1883– (Contains references to all current medical literature, and reviews of much of it).
Journal of the Canadian Medical Association, Toronto, 1911–
Journal of Economic Entomology, Geneva, N. Y., 1908–
Journal of Experimental Medicine, New York, 1896–
Journal of Infectious Diseases, Chicago.
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